CLAIMS

1. Use of an NPR-B agonist in the manufacture of a medicament for the treatment of a thoracolumbar deformity in a human subject with achondroplasia wherein the human subject has or is at risk of developing said thoracolumbar deformity.

2. The use according to claim 1, wherein said use is for the treatment of thoracolumbar kyphosis in said human subject.

3. The use according to claim 1 or 2, wherein said use comprises the step of measuring the spinal deformity prior to, and optionally during and/or subsequent to said treatment.

4. The use according to any one of claims 1 to 3, wherein said use comprises successive administrations of the NPR-B agonist to said subject, over a treatment period of at least about 6 months or at least about 1 year, such as daily, weekly, biweekly or monthly, during said treatment period.

5. The use according to any one of claims 1 to 4, wherein said use comprises measuring the thoracolumbar deformity prior to said treatment, and/or about every 3 months, or about every 6 months, or about every 9 months, or about yearly, during said treatment or treatment period.

6. The use according to any one of claims 1 to 5, wherein said use comprises measuring the degree of thoracolumbar kyphosis, in the subject, prior to, and optionally during and/or subsequent to said treatment.

7. The use according to any one of claims 1 to 6, wherein said use further comprises measuring the degree of lordosis, such as lumbar lordosis, in the subject, prior to, and optionally during and/or subsequent to said treatment.

8. The use according to any one of claims 1 to 7, wherein said use is for the treatment of a thoracolumbar deformity which comprises a vertebral morphology deformity, such as gibbus deformity, wherein said treatment results in an improvement in the vertebral morphology.

9. The use according to any one of claims 1 to 8, wherein said use further comprises the step of measuring vertebral morphology, prior to and during said treatment period, such as using vertebral morphometry, such as point morphometry of one or more vertebra, such as a thoracic and/or lumbar vertebra, such as vertebral morphometry of vertebra L1 and/or L2, wherein optionally said treatment results in a decrease in the PH/MW ratio of vertebra L1 and/or L2.

10. The use according to any one of claims 1 to 9, wherein said use results in a reduction or normalization of gibbis deformity, such as gibbis deformity of vertebra L1, L2 or L1 and L2.

11. The use according to any one of claims 1 to 10, wherein said use results in a reduction or normalization of the thoracolumbar kyphosis Cobb angle, such as the thoracolumbar kyphosis Cobb Angle measured between vertebra T10 – L2 or T11 – L2 or T12 – L2.

12. The use according to any one of claims 1 to 11, wherein prior to said use or treatment the subject has a thoracolumbar kyphosis Cobb Angle of greater than about 20°, or greater than about 25°, or greater than about 30°, or greater than about 35°, or greater than about 40°, or greater than about 45°, or greater than about 50°.

13. The use according to any one of claims 1 to 12, wherein said use results in a reduction or normalization in the thoracolumbar kyphosis Cobb Angle, such as a reduction or normalization in the thoracolumbar kyphosis Cobb angle of at least 3°, such as at least about 3° over a treatment period of at least about 6 months treatment period, or at least about 12 months treatment period; or a reduction in the Achondroplasia thoracolumbar kyphosis related Z-Score or a reduction in the Healthy thoracolumbar kyphosis Z-Score.

14. The for use according to any one of claims 1 to 13, wherein said use comprises the measurement of said thoracolumbar deformity prior to and/or during said treatment using spinal radiography, such as a lateral spinal radiography, wherein optionally, said spinal radiography is taken from the subject whilst standing, or whilst sitting, or from a supine position or from an image or radiograph taken from the subject whilst standing, or whilst sitting, or from a supine position.

15. The use according to any one of claims 1 to 14, wherein said use is for treatment of a thoracolumbar deformity in a subject who is a child, such as a child of age 0 to 18 years of age, such as a child of age 0 to 14 years of age, such as a child of less than 12 years of age such as less than 10 years of age or less than 8 years of age or less than 6 years of age, such as a child of less than 5 years of age.

16.The use according to any one of claims 1 to 15, wherein said use is for treatment of a thoracolumbar deformity in a subject who prior to and during the treatment or treatment period, has open bone epiphysis.

17. The use according to any one of claims 1 to 16, wherein said use is for treatment of unfixed thoracolumbar kyphosis.

18. The use according to any one of claims 1 to 14, wherein said use is for treatment of a subject who has closed bone epiphysis.

19. The use according to any one of claims 1 to 14 or claim 18, wherein said use is for treatment of a subject who is at least 18 years of age, such as at least 25 years of age, such as at least 30 years of age.

20. The use according to any one of claims 1 to 16, 18 or 19, wherein said use is for the treatment of fixed thoracolumbar kyphosis.

21. The use according to any one of claims 1 to 20, wherein said use is for increasing height velocity, such as annualized growth velocity (AGV), or rate of linear growth in the subject, or achondroplasia related height Z-Score.

22. The use according to any one of claims 1 to 21, wherein said use is further for use in increasing muscle function or physical functioning of said subject, such as for use in one or more of

a) increased skeletal muscle strength,

b) increased skeletal muscle tone,

c) increased skeletal muscle stamina,

d) increased skeletal muscle mass,

e) decreased skeletal muscle fatigue,

f) increased cardiovascular endurance,

g) increased cardiovascular fitness,

h) decreased exercise intolerance,

i) increased exercise capacity,

j) decreased exercise induced fatigue, and

k) decreased hypotonia.

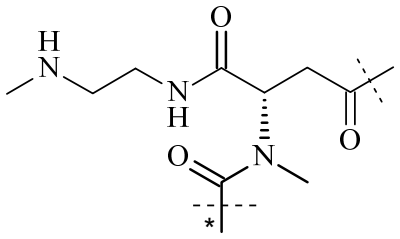
23. The use according to any one of claims 1to 22, wherein said use is, or is also, for enhancing physical functioning or daily living functioning of said subject, which may optionally be assessed via one or more of (i) ACEM-OSM (ii) ACEM-Physical Functioning (iii) ACEM-Daily Living Functioning and (iv) SF-10 Physical Functioning.

24. The use according to any one of claims 1 to 23, wherein said use further comprises the use of a spinal support or spinal brace, such as thoracolumbosacral orthosis (TLSO), prior to, during, or subsequent to said treatment/treatment period.

25. The use according to any one of claims 1 to 24, wherein the NPR-B agonist is or comprises a C-type natriuretic peptide (CNP), a CNP conjugate or a CNP prodrug; or a pharmaceutically acceptable salt thereof.

26. The use according to any one of claims 1 to 25, wherein in said use the NPR-B agonist is:

(a) a compound of formula (IIf ’):

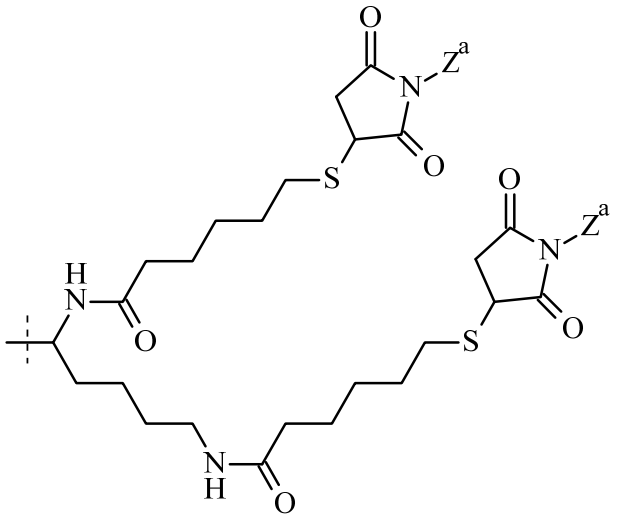


(IIf ’),

wherein

the unmarked dashed line indicates the attachment to a nitrogen provided by the side chain of the lysine at position 26 of the CNP moiety of SEQ ID NO:24 by forming an amide bond; and

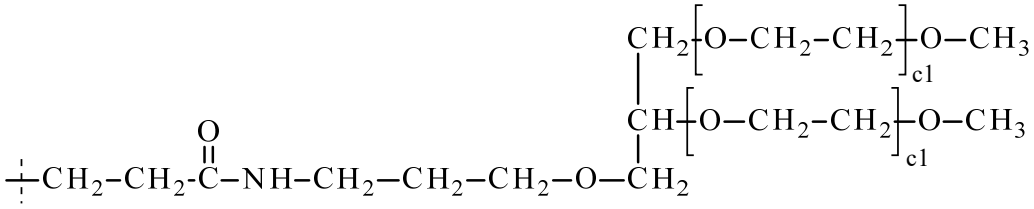
the dashed line marked with the asterisk indicates attachment to -Z having the structure



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wherein

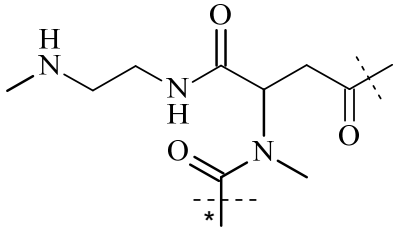
each -Z^a is



wherein

each c1 is an integer independently ranging from 200 to 250;

(b) a compound of formula (IIf):

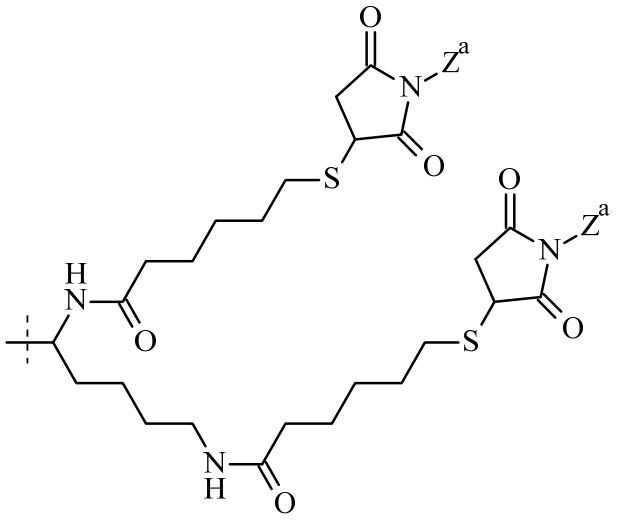


(IIf),

wherein

the unmarked dashed line indicates the attachment to a nitrogen of -D which is a CNP moiety by forming an amide bond; and

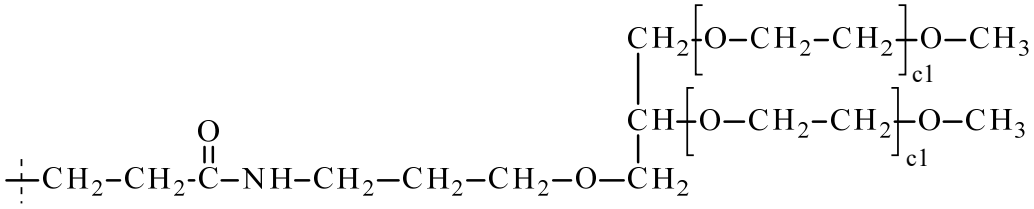
the dashed line marked with the asterisk indicates attachment to -Z having the structure



,

wherein

each -Z^a is

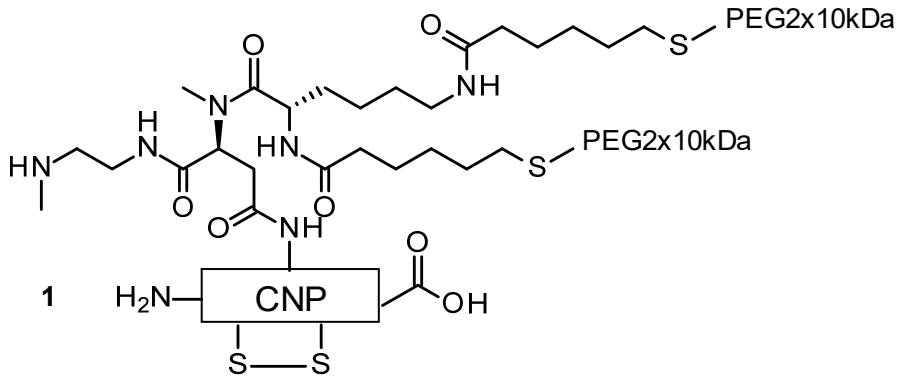


wherein

each c1 is an integer independently ranging from 200 to 250;

(c) Navepegritide;

(d) compound (1):



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or a pharmaceutically acceptable salt thereof, wherein optionally the NPR-B agonist is to be administered weekly.

27. The use according to any one of claims 1 to 25, wherein in said use the NPR-B agonist is or comprises vosoritide (SEQ ID NO:30), wherein optionally the NPR-B agonist is to be administered daily.

28. The use according to any one of claims 1 to 27, wherein the subject has or has been diagnosed with a developmental delay, such as developmental motor delay, and/or a cranial abnormality, such as a narrowing of the occipital foramen or foramen magnum compression.