

CLAIMS

1. A soluble fibroblast growth factor receptor 3 (sFGFR3) polypeptide comprising an amino acid sequence with at least 99% sequence identity to SEQ ID NO: 33.
2. An sFGFR3 polypeptide according to Claim 1, in which the sFGFR3 polypeptide
5 comprises an amino acid sequence of SEQ ID NO: 33.
3. An sFGFR3 polypeptide according to Claim 1 or 2, in which the sFGFR3 polypeptide binds to at least one of fibroblast growth factor 1 (FGF1), fibroblast growth factor 2 (FGF2), fibroblast growth factor 9 (FGF9), fibroblast growth factor 18 (FGF18), fibroblast growth factor 19 (FGF19), or fibroblast growth factor 21 (FGF21).
- 10 4. An sFGFR3 polypeptide according to Claim 1 or 2, in which the sFGFR3 polypeptide binds to fibroblast growth factor 1 (FGF1), fibroblast growth factor 2 (FGF2), fibroblast growth factor 9 (FGF9), and fibroblast growth factor 18 (FGF18).
5. An sFGFR3 polypeptide according to any preceding claim, in which the binding is characterized by an equilibrium dissociation constant (Kd) of from 0.2 nM to 20 nM.
- 15 6. An sFGFR3 polypeptide according to any of Claims 1 to 4, in which the binding is characterized by a Kd of from 1 nM to 10 nM.
7. An sFGFR3 polypeptide according to any preceding claim, in which the sFGFR3 polypeptide is encoded by nucleotides 52-1098 of SEQ ID NO: 21.
8. A composition comprising:
20 a soluble fibroblast growth factor receptor 3 (sFGFR3) polypeptide comprising an amino acid sequence of SEQ ID NO: 33; and
a pharmaceutically acceptable excipient.
9. An sFGFR3 polypeptide according to Claim 8, in which the composition comprises less than 2% aggregation of the sFGFR3 polypeptide.
- 25 10. A soluble fibroblast growth factor receptor 3 (sFGFR3) polypeptide according to any of Claims 1 to 7 or a composition according to Claim 8 or 9 for use in treating an FGFR3-related skeletal growth retardation disorder in a subject, in which the FGFR3-related skeletal growth retardation disorder is associated with gain-of-function mutation in FGFR3.

11. An sFGFR3 polypeptide or a composition for use according to Claim 10, in which the FGFR3-related skeletal disease is achondroplasia, thanatophoric dysplasia type I (TDI), thanatophoric dysplasia type II (TDII), severe achondroplasia with developmental delay and acanthosis nigricans (SADDAN), hypochondroplasia or a craniosynostosis syndrome.
- 5 12. An sFGFR3 polypeptide or a composition for use according to Claim 11, in which the skeletal growth retardation disorder is achondroplasia.
13. An sFGFR3 polypeptide or a composition for use according to Claim 11, in which the skeletal growth retardation disorder is hypochondroplasia.
- 10 14. An sFGFR3 polypeptide or a composition for use according to any of Claims 10 to 13, in which treating the FGFR3-related skeletal growth retardation disorder in a subject comprises improving one or more symptoms in the subject.
15. An sFGFR3 polypeptide or a composition for use according to any of Claims 10 to 14, in which the subject is to be administered a dose of the polypeptide of 0.002 mg/kg to 30 mg/kg.
- 15 16. An sFGFR3 polypeptide or a composition for use according to any of Claims 10 to 15, in which the subject is to be administered a dose of the polypeptide of 0.2 mg/kg to 3 mg/kg.
17. An sFGFR3 polypeptide or a composition for use according to any of Claims 10 to 16, in which treating the FGFR3-related skeletal growth retardation disorder in a subject comprises:
- 20 (a) increasing survival of the subject;
- (b) improving locomotion of the subject;
- (c) improving abdominal breathing in the subject;
- (d) increasing body and/or bone length of the subject; or
- (e) improving the cranial ratio and/or restores foramen magnum shape in the subject.
- 25 18. An sFGFR3 polypeptide or a composition for use according to any of Claims 10 to 17, in which the polypeptide or composition is to be administered subcutaneously.
19. An sFGFR3 polypeptide or a composition for use according to any of Claims 10 to 17, in which the polypeptide or composition is to be administered intravenously.

20. An sFGFR3 polypeptide or a composition for use according to any of Claims 10 to 19, in which the subject has not been previously administered the pharmaceutical composition.

21. An sFGFR3 polypeptide or a composition for use according to any of Claims 10 to 20, in which the subject is selected from the group consisting of an infant, a child, and an adult.

5 22. An sFGFR3 polypeptide or a composition for use according to any of Claims 10 to 21, in which the subject is a human.

23. A composition for use in treating achondroplasia in a human subject, in which the composition comprises:

10 a soluble fibroblast growth factor receptor 3 (sFGFR3) polypeptide comprising an amino acid sequence of SEQ ID NO: 33; and
a pharmaceutically acceptable excipient.

CLAIMS

1. A soluble fibroblast growth factor receptor 3 (sFGFR3) polypeptide comprising the amino acid sequence of SEQ ID NO: 33.
2. An sFGFR3 polypeptide according to Claim 1, in which the sFGFR3 polypeptide binds to at least one of fibroblast growth factor 1 (FGF1), fibroblast growth factor 2 (FGF2), fibroblast growth factor 9 (FGF9), fibroblast growth factor 18 (FGF18), fibroblast growth factor 19 (FGF19), or fibroblast growth factor 21 (FGF21).
3. An sFGFR3 polypeptide according to Claim 1, in which the sFGFR3 polypeptide binds to fibroblast growth factor 1 (FGF1), fibroblast growth factor 2 (FGF2), fibroblast growth factor 9 (FGF9), and fibroblast growth factor 18 (FGF18).
4. An sFGFR3 polypeptide according to Claim 1, 2 or 3, in which the binding is characterized by an equilibrium dissociation constant (Kd) of from 0.2 nM to 20 nM.
5. An sFGFR3 polypeptide according to any preceding claim, in which the binding is characterized by a Kd of from 1 nM to 10 nM.
6. An sFGFR3 polypeptide according to any preceding claim, in which the sFGFR3 polypeptide is encoded by nucleotides 52-1098 of SEQ ID NO: 21.
7. A composition comprising:
 - a soluble fibroblast growth factor receptor 3 (sFGFR3) polypeptide comprising an amino acid sequence of SEQ ID NO: 33; and
 - a pharmaceutically acceptable excipient.
8. A composition according to Claim 7, in which the composition comprises less than 2% aggregation of the sFGFR3 polypeptide.
9. A soluble fibroblast growth factor receptor 3 (sFGFR3) polypeptide according to any of Claims 1 to 6 or a composition according to Claim 7 or 8 for use in treating an FGFR3-related skeletal growth retardation disorder in a subject, in which the FGFR3-related skeletal growth retardation disorder is associated with gain-of-function mutation in FGFR3.
10. An sFGFR3 polypeptide or a composition for use according to Claim 9, in which the FGFR3-related skeletal disease is achondroplasia, thanatophoric dysplasia type I (TDI),

thanatophoric dysplasia type II (TDII), severe achondroplasia with developmental delay and acanthosis nigricans (SADDAN), hypochondroplasia or a craniosynostosis syndrome.

11. An sFGFR3 polypeptide or a composition for use according to Claim 10, in which the skeletal growth retardation disorder is achondroplasia.

5 12. An sFGFR3 polypeptide or a composition for use according to Claim 10, in which the skeletal growth retardation disorder is hypochondroplasia.

13. An sFGFR3 polypeptide or a composition for use according to any of Claims 9 to 12, in which treating the FGFR3-related skeletal growth retardation disorder in a subject comprises improving one or more symptoms in the subject.

10 14. An sFGFR3 polypeptide or a composition for use according to any of Claims 9 to 13, in which the subject is to be administered a dose of the polypeptide of 0.002 mg/kg to 30 mg/kg.

15. An sFGFR3 polypeptide or a composition for use according to any of Claims 9 to 14, in which the subject is to be administered a dose of the polypeptide of 0.2 mg/kg to 3 mg/kg.

15 16. An sFGFR3 polypeptide or a composition for use according to any of Claims 9 to 15, in which treating the FGFR3-related skeletal growth retardation disorder in a subject comprises:

- (a) increasing survival of the subject;
- (b) improving locomotion of the subject;
- (c) improving abdominal breathing in the subject;
- (d) increasing body and/or bone length of the subject; or

20 (e) improving the cranial ratio and/or restores foramen magnum shape in the subject.

17. An sFGFR3 polypeptide or a composition for use according to any of Claims 9 to 16, in which the polypeptide or composition is to be administered subcutaneously.

18. An sFGFR3 polypeptide or a composition for use according to any of Claims 9 to 16, in which the polypeptide or composition is to be administered intravenously.

25 19. An sFGFR3 polypeptide or a composition for use according to any of Claims 9 to 18, in which the subject has not been previously administered the pharmaceutical composition.

20. An sFGFR3 polypeptide or a composition for use according to any of Claims 9 to 19, in which the subject is selected from the group consisting of an infant, a child, and an adult.
21. An sFGFR3 polypeptide or a composition for use according to any of Claims 9 to 20, in which the subject is a human.
- 5 22. A composition for use in treating achondroplasia in a human subject, in which the composition comprises:
 - a soluble fibroblast growth factor receptor 3 (sFGFR3) polypeptide comprising an amino acid sequence of SEQ ID NO: 33; and
 - a pharmaceutically acceptable excipient.