Others have reported on various sustained release GH preparations (Cook DM, et al. 2002. J Clin Endocrinol Metab 87(10):4508-4514; Biller BM, et al. 2011. J Clin Endocrinol Metab 96(6):1718-1726; Peter F. et al., 2012. J Clin Endocrinol Metab 97(2):400-407; Fares F. et al, 2010. Endocrinology 151(9):4410-4417; Sondergaard E, et al. 2011. J Clin Endocrinol Metab 96(3):681-688; de Schepper J et al. 2011. European Journal of Endocrinology 165(3):401-409; Bidlingmaier M, et al. 2006. J Clin Endocrinol Metab 91(8):2926-2930). However, there remains a need for alternative GH therapeutics, dosages, and treatment regimens.

VRS-317 is an investigational long-acting rhGH in development for long-term replacement therapy for adults with GHD and children with pediatric GHD. VRS-317 was designed to achieve up to once-monthly dosing with the anticipation that a reduced frequency of administration (as few as 12 versus up to 365 injections per year) would increase treatment adherence and thereby improve overall treatment outcomes. VRS-317 is an rhGH fusion protein that was designed to minimize receptor mediated clearance through a reduction in receptor binding achieved without mutations to rhGH by genetically fusing extended recombinant polypeptide (XTEN) amino acid sequences to the N- and C-termini of the native hGH sequence (Cleland et al. 2012, Journal of Pharmaceutical Sciences. 101(8):2744-2754, Epub 2012 Jun 7).

SUMMARY OF THE INVENTION

The present invention concerns an improved therapeutic regimen for pediatric growth hormone deficiency ("PGHD") therapy in children. In particular, the invention concerns methods for bolus dose administration of compositions of fusion proteins comprising human growth hormone fused to one or more extended recombinant polypeptides (XTEN) (the fusion protein hereinafter referred to as "hGH-XTEN"). Accordingly, in one aspect, the present invention concerns a method of treating pediatric patients having human PGHD with an hGH-XTEN fusion protein.

In one aspect, there is provided a use of a human growth hormone-XTEN (hGH-XTEN) fusion protein comprising an amino acid sequence having at least about 90% sequence identity to SEQ ID NO:1 in the manufacture of a medicament for treating human pediatric growth hormone deficiency (PGHD) in a pediatric patient, wherein the hGH-XTEN fusion protein is prepared for administering to the pediatric patient with

PGHD as a therapeutically effective bodyweight adjusted bolus dose between about 0.80 mg/kg and about 6.3 mg/kg.

In one aspect, there is provided a use of a human growth hormone-XTEN (hGH-XTEN) fusion protein comprising an amino acid sequence having at least about 90% sequence identity to SEQ ID NO:1 in the manufacture of a medicament for treating human pediatric growth hormone deficiency (PGHD) in a human pediatric patient, wherein the hGH-XTEN fusion protein is prepared for administering to the patient with PGHD as a therapeutically effective bodyweight adjusted bolus dose that is effective to maintain the patient's serum IGF-I standard deviation score (SDS) between about -2.0 and about 2.0 for at least 7 days after administration of the bolus dose.

In one aspect, there is provided a pediatric bolus dose of an hGH-XTEN fusion protein comprising an amino acid sequence having at least about 90% sequence identity to SEQ ID NO:1, wherein the bolus dose is a therapeutically effective bodyweight adjusted bolus dose comprising between about 0.8 mg/kg and about 6.3 mg/kg of hGH-XTEN fusion protein.

In one aspect, there is provided a kit for the treatment of pediatric growth hormone deficiency (PGHD) comprising

(i) a container which holds a pharmaceutical composition comprising a human growth hormone-XTEN (hGH-XTEN) fusion protein comprising an amino acid sequence having at least about 90% sequence identity to SEQ ID NO:1, and

(ii) a package insert associated with said container, wherein the package insert indicates that said composition is for the treatment of pediatric growth hormone deficiency (PGHD) in a pediatric patient by administration of an initial dose of the hGH-XTEN fusion protein between about 0.8 mg/kg and about 6.3 mg/kg and a plurality of subsequent doses of the hGH-XTEN fusion protein between about 0.8 mg/kg and about 6.3 mg/kg, wherein the doses are administered once a month, twice a month, three times a month, or four times a month.

In one aspect, the present invention provides a method of treating human pediatric growth hormone deficiency (PGHD) in a pediatric patient by administering to the patient with PGHD a dose of human growth hormone-XTEN (hGH-XTEN) fusion protein. In another embodiment, the hGH-XTEN fusion protein comprises an amino acid sequence having at least about 90% sequence identity to SEQ ID NO:1. In one other embodiment, the dose is a bolus dose. In one embodiment, the bolus dose of hGH-XTEN is a

WHAT IS CLAIMED IS:

1. A method of treating human pediatric growth hormone deficiency (PGHD) in a pediatric patient, comprising administering to the pediatric patient with PGHD a human growth hormone-XTEN (hGH-XTEN) fusion protein comprising an amino acid sequence having at least about 90% sequence identity to SEQ ID NO:1, as a therapeutically effective bodyweight adjusted bolus dose between about 0.80 mg/kg and about 6.3 mg/kg.

2. The method of claim 1, wherein the bolus dose is administered every week, every two weeks, semimonthly, every three weeks, or monthly.

3. The method of claim 2, wherein the bolus dose is administered monthly.

4. The method of claim 2, wherein the bolus dose is administered every two weeks or semimonthly.

5. The method of any one of claims 1 to 4, wherein the bolus dose is administered subcutaneously.

6. The method of any one of claims 1 to 5, wherein the method is effective to achieve a height velocity equivalent to 7 cm/yr to 12 cm/yr in a pediatric patient.

7. The method of any one of claims 1 to 5, wherein the method is effective to achieve a height velocity equivalent to 8 cm/yr to 11 cm/yr in a pediatric patient.

8. The method of claims 6 or 7, wherein the height velocity is achieved after at least 3 months, at least 6 months, or at least 12 months of dosing in the pediatric patient.

9. The method of claims 6 or 7, wherein the height velocity achieved is a first year height velocity.

10. The method of any one of claims 1 to 5, wherein the method is not inferior to achieve a height velocity in a pediatric patient compared with that achieved using daily injections of hGH not linked to XTEN over the same period.

11. The method of any one of claims 6 to 10, wherein the bolus dose is selected from about 0.8 mg/kg to about 1.5 mg/kg, about 1.8 mg/kg to about 3.2 mg/kg, or about 3.5 mg/kg to about 6.3 mg/kg.

12. The method of any one of claims 1 to 11, wherein the pediatric patient maintains an increase from baseline serum IGF-I standard deviation score (SDS) of at least 1.0 for at least about 7 days, at least about 8 days, at least about 9 days, at least about 10 days, at least about 11 days, at least about 12 days, at least about 13 days, at least about 14 days, at least about 15 days, at least about 16 days, at least about 17 days, at least about 18 days, at least about 19 days, at least about 20 days, at least about 21 days, at least about 22 days, at least about 23 days, at least about 24 days, at least about 25 days, at least about 26 days, at least about 27 days, at least about 28 days, at least about 29 days, at least about 30 days, or at least about one month following administration.

13. The method of any one of claims 1 to 11, wherein the pediatric patient maintains an increase from baseline serum IGF-I standard deviation score (SDS) of at least 1.0 for at least about 14 days, at least about 21 days, or at least about 30 days following administration.

14. The method of any one of claims 1 to 11, wherein the pediatric patient maintains an increase from baseline serum IGF-I standard deviation score (SDS) of at least 1.0 for at least about 14 days, or at least about 30 days following administration.

15. The method of any one of claims 1 to 11, wherein the pediatric patient has a serum IGF-I standard deviation score (SDS) between about -2.0 and about 2.0 following administration.

16. The method of claim 15, wherein the IGF-I SDS is selected from the group consisting of greater than about -1.5 to about 2.0, greater than about -1.0 to about 2.0, greater than about -0.5 to about 2.0, greater than about 0 to about 2.0, greater than about 0.5 to about 2.0, greater than about 1.0 to about 2.0, and greater than about 1.5 to about 2.0.

17. The method of claim 15, wherein the IGF-I SDS is selected from the group consisting of greater than about -1.0 to about 2.0, greater than about 0 to about 2.0, and greater than about 1.0 to about 2.0.

18. The method of claim 15, wherein the pediatric patient exhibits said serum IGF-I SDS following administration of the bolus dose, wherein the administration is weekly, every two weeks, semimonthly, every three weeks, or monthly.

19. The method of claim15, wherein the pediatric patient exhibits said serum IGF-I SDS following administration of the bolus dose, wherein the administration is semimonthly, or monthly.

20. The method of any one of claims 12 to 19, wherein the pediatric patient exhibits said serum IGF-I SDS following administration of at least a second, or a third, or a fourth bolus dose.

21. The method of claim 15, wherein the bolus dose is effective to maintain the pediatric patient's serum IGF-I SDS between about -2.0 and about 2.0 for at least about 7 days, at least about 8 days, at least about 9 days, at least about 10 days, at least about 11 days, at least about 12 days, at least about 13 days, at least about 14 days, at least about 15 days, at least about 16 days, at least about 17 days, at least about 18 days, at least about 19 days, at least about 20 days, at least about 21 days, at least about 22 days, at least about 23 days, at least about 24 days, at least about 25 days, at least about 26 days, at least about 27 days, at least about 28 days, at least about 29 days, at least about 30 days, or at least about one month following administration.

22. The method of claim 21, wherein the bolus dose is effective to maintain the pediatric patient's serum IGF-I SDS between about -2.0 and about 2.0 for at least about 14 days, at least about 21 days, or at least about 30 days following administration.

23. The method of claim 21, wherein the bolus dose is effective to maintain the pediatric patient's serum IGF-I SDS between about -2.0 and about 2.0 for at least about 14 days, or at least about 30 days following administration.

24. The method of any one of claims 21 to 23, wherein the IGF-I SDS is maintained between about -2.0 and about 2.0 following administration of a first, or a second, or a third, or a fourth bolus dose.

25. The method of any one of claims 1 to 24, wherein the bolus dose is selected from the group consisting of about 0.8 mg/kg, about 1.0 mg/kg, about 1.2 mg/kg, about 1.4 mg/kg, about 1.6 mg/kg, about 1.8 mg/kg, about 2.0 mg/kg, about 2.2 mg/kg, about 2.4 mg/kg, about 2.6 mg/kg, about 2.7 mg/kg, about 2.8 mg/kg, about 3 mg/kg, about 3.2 mg/kg, about 3.4 mg/kg, about 3.6 mg/kg, about 3.8 mg/kg, about 4.0 mg/kg, about 4.2 mg/kg, about 4.4 mg/kg, about 4.6 mg/kg, about 4.8 mg/kg, about 5.0 mg/kg, about 5.2 mg/kg, about 5.4 mg/kg, about 5.6 mg/kg, about 5.8 mg/kg, about 6.0 mg/kg, and about 6.3 mg/kg.

26. The method of any one of claims 1 to 24, wherein the bolus dose is about 0.8 mg/kg to about 1.5 mg/kg.

27. The method of any one of claims 1 to 24, wherein the bolus dose is about 1.8 mg/kg to about 3.2 mg/kg.

28. The method of any one of claims 1 to 24, wherein the bolus dose is about 3.5 mg/kg to about 6.3 mg/kg.

29. The method of any one of claims 1 to 28, wherein the hGH-XTEN fusion protein comprises the amino acid sequence of SEQ ID NO:1.

30. The method of any one of claims 1 to 28, wherein the hGH-XTEN fusion protein has at least about 91%, or at least about 92%, or at least about 93%, or at least about 94%, or at least about 95%, or at least about 96%, or at least about 97%, or at least about 98%, or at least about 99% sequence identity to SEQ ID NO:1.

31. A method of treating human pediatric growth hormone deficiency (PGHD) in a human pediatric patient, comprising administering to the patient with PGHD a human growth hormone-XTEN (hGH-XTEN) fusion protein comprising an amino acid sequence

having at least about 90% sequence identity to SEQ ID NO:1 as a therapeutically effective bodyweight adjusted bolus dose that is effective to maintain the patient's serum IGF-I standard deviation score (SDS) between about -2.0 and about 2.0 for at least 7 days after administration of the bolus dose.

32. The method of claim 31, wherein the bolus dose is between about 0.8 mg/kg and about 6.3 mg/kg.

33. The method of claim 31 or 32, wherein said bolus dose is effective to maintain the patient's serum IGF-I SDS between about -2.0 and about 2.0 for at least about 7 days, at least about 8 days, at least about 9 days, at least about 10 days, at least about 11 days, at least about 12 days, at least about 13 days, at least about 14 days, at least about 15 days, at least about 16 days, at least about 17 days, at least about 18 days, at least about 19 days, at least about 20 days, at least about 21 days, at least about 22 days, at least about 23 days, at least about 24 days, at least about 25 days, at least about 26 days, at least about 27 days, at least about 28 days, at least about 29 days, at least about 30 days, or at least about one month following administration.

34. The method of claim 33, wherein the bolus dose is effective to maintain the pediatric patient's serum IGF-I SDS between about -2.0 and about 2.0 for at least about 14 days, at least about 21 days, or at least about 30 days following administration.

35. The method of claim 33, wherein the bolus dose is effective to maintain the pediatric patient's serum IGF-I SDS between about -2.0 and about 2.0 for at least about 14 days, or at least about 30 days following administration.

36. A pediatric bolus dose of an hGH-XTEN fusion protein comprising an amino acid sequence having at least about 90% sequence identity to SEQ ID NO:1, wherein the bolus dose is a therapeutically effective bodyweight adjusted bolus dose comprising between about 0.8 mg/kg and about 6.3 mg/kg of hGH-XTEN fusion protein.

37. The bolus dose of claim 36 for use in treating human pediatric growth hormone deficiency (PGHD) in a pediatric patient in need.

38. The bolus dose of claims 36 or 37, wherein the hGH-XTEN fusion protein comprises the amino acid sequence of SEQ ID NO:1.

39. The bolus dose of any one of claims 36 to 38, which is formulated for subcutaneous administration.

40. An hGH-XTEN fusion protein comprising an amino acid sequence having at least about 90% sequence identity to SEQ ID NO:1 for use in a method for the treatment of human pediatric growth hormone deficiency (PGHD) in a human pediatric patient, wherein the method comprises administering a therapeutically effective bodyweight adjusted bolus dose of the hGH-XTEN fusion protein at a dose between about 0.8 mg/kg and about 6.3 mg/kg.

41. Use of an hGH-XTEN fusion protein comprising an amino acid sequence having at least about 90% sequence identity to SEQ ID NO:1 in the manufacture of a medicament for the treatment of PGHD in a pediatric patient, wherein the hGH-XTEN fusion protein is administered to the pediatric patient as a therapeutically effective bodyweight adjusted bolus dose of the hGH-XTEN fusion protein at a dose between about 0.8 mg/kg and about 6.3 mg/kg.

42. The hGH-XTEN fusion protein of claim 40 or the use of claim 41, wherein the bolus dose is administered every week, every two weeks, semimonthly, every three weeks, or monthly.

43. The hGH-XTEN fusion protein of claim 40 or the use of claim 41, wherein the bolus dose is administered semimonthly, or monthly.

44. The hGH-XTEN fusion protein of claim 40 or the use of any one of claims 41 to 43, wherein the hGH-XTEN fusion protein comprises the amino acid sequence of SEQ ID NO:1.

45. The hGH-XTEN fusion protein of claim 40 or the use of any one of claims 41 to 44, wherein the bolus dose is administered subcutaneously.

46. The hGH-XTEN fusion protein of claim 40 or the use of any one of claims 41 to 45, wherein the human pediatric patient has a serum IGF-I standard deviation score (SDS) between about -2.0 and about 2.0 following administration of the bolus dose.

47. The hGH-XTEN fusion protein of claim 40 or the use of claim 46, wherein the IGF-I SDS is selected from the group consisting of greater than about -1.5, greater than about -1.0, greater than about -0.5, greater than about 0, greater than about 0.5, greater than about 1.0, and greater than about 1.5.

48. The hGH-XTEN fusion protein of claim 40 or the use of claim 46, wherein the IGF-I SDS is selected from the group consisting of greater than about -1.0, greater than about 0, and greater than about 1.0.

49. The hGH-XTEN fusion protein of claim 40 or the use of any one of claims 41 to 48, wherein the administration is weekly, every two weeks, semimonthly, every three weeks, or monthly.

50. The hGH-XTEN fusion protein of claim 40 or the use of any one of claims 41 to 48, wherein the administration is semimonthly, or monthly.

51. A kit for the treatment of pediatric growth hormone deficiency (PGHD) comprising

(i) a container which holds a pharmaceutical composition comprising a human growth hormone-XTEN (hGH-XTEN) fusion protein comprising an amino acid sequence having at least about 90% sequence identity to SEQ ID NO:1, and

(ii) a package insert associated with said container, wherein the package insert indicates that said composition is for the treatment of pediatric growth hormone deficiency (PGHD) in a pediatric patient by administration of an initial dose of the hGH-XTEN fusion protein between about 0.8 mg/kg and about 6.3 mg/kg and a plurality of subsequent doses of the hGH-XTEN fusion protein between about 0.8 mg/kg and about 6.3 mg/kg, wherein the doses are administered every week, every two weeks, semimonthly, every three weeks, or monthly.

52. The kit of claim 51, wherein the container further comprises a pharmaceutically acceptable carrier.

53. A human growth hormone-XTEN (hGH-XTEN) fusion protein comprising an amino acid sequence having at least about 90% sequence identity to SEQ ID NO:1 for use in a pharmaceutical regimen for treatment of a treatment of pediatric growth hormone deficiency (PGHD) in a pediatric patient, said regimen comprising administering a bolus dose of the hGH-XTEN fusion protein to treat the pediatric patient.

54. The hGH-XTEN fusion protein of claim 53, wherein the pharmaceutical regimen further comprises the step of determining the amount of hGH-XTEN fusion protein needed to achieve an IGF-I standard deviation score (SDS) between about -2.0 and about 2.0 in the pediatric patient.

55. The hGH-XTEN fusion protein of claim 53, wherein the pharmaceutical regimen for treating the pediatric patient comprises administering the hGH-XTEN fusion protein in an initial bolus dose between about 0.8 mg/kg and about 6.3 mg/kg and a plurality of subsequent bolus doses of the hGH-XTEN fusion protein between about 0.8 mg/kg and about 6.3 mg/kg.

56. The hGH-XTEN fusion protein of claim 55, wherein the bolus doses are administered every week, every two weeks, semimonthly, every three weeks, or monthly.

57. The hGH-XTEN fusion protein of claim 55, wherein the bolus doses are administered semimonthly, or monthly.

58. The method of claim 10, wherein the hGH-XTEN fusion protein administered is comparable, on a molar basis, to an equivalent amount of an hGH not linked to XTEN and administered to a pediatric patient.

59. The method of any one of claims 1 to 5, wherein the method is effective to maintain the pediatric patient's height velocity within at least about 10%, at least about 20%, or at least about 30% of that compared to the height velocity achieved in pediatric

patients administered daily injections of hGH not linked to XTEN of an equivalent amount, on a molar basis, over a comparable dose period.

WHAT IS CLAIMED IS:

1. Use of a human growth hormone-XTEN (hGH-XTEN) fusion protein comprising an amino acid sequence having at least about 90% sequence identity to SEQ ID NO:1 in the manufacture of a medicament for treating human pediatric growth hormone deficiency (PGHD) in a pediatric patient, wherein the hGH-XTEN fusion protein is prepared for administering to the pediatric patient with PGHD as a therapeutically effective bodyweight adjusted bolus dose between about 0.80 mg/kg and about 6.3 mg/kg.

2. The use of claim 1, wherein the bolus dose is administered once a month, twice a month, three times a month, or four times a month.

3. The use of claim 2, wherein the bolus dose is administered monthly.

4. The use of claim 2, wherein the bolus dose is administered every two weeks or semimonthly.

5. The use of claim 1 or claim 2, wherein the bolus dose is administered subcutaneously.

6. The use of claim 2, wherein the method is effective to achieve a height velocity equivalent to 7 cm/yr to 12 cm/yr in a pediatric patient.

7. The use of claim 2, wherein the method is effective to achieve a height velocity equivalent to 8 cm/yr to 11 cm/yr in a pediatric patient.

8. The use of claims 6 or 7, wherein the height velocity is achieved after at least 3 months, at least 6 months, or at least 12 months of dosing in the pediatric patient.

9. The use of claims 6 or 7, wherein the height velocity achieved is a first year height velocity.

10. The use of claim 2, wherein the method is not inferior to achieve a height velocity in a pediatric patient compared with that achieved using daily injections of hGH not linked to XTEN over the same period.

11. The use of claim 6 or claim 7, wherein the bolus dose is selected from about 0.8 mg/kg to about 1.5 mg/kg, about 1.8 mg/kg to about 3.2 mg/kg, or about 3.5 mg/kg to about 6.3 mg/kg.

13. The use of claim 1, wherein the pediatric patient maintains an increase from baseline serum IGF-I standard deviation score (SDS) of at least 1.0 for at least about 7 days, at least about 14 days, at least about 21 days, or at least about 30 days following administration.

14. The use of claim 1, wherein the pediatric patient maintains an increase from baseline serum IGF-I standard deviation score (SDS) of at least 1.0 for at least about 14 days, or at least about 30 days following administration.

15. The use of claim 1, wherein the pediatric patient has a serum IGF-I standard deviation score (SDS) between about -2.0 and about 2.0 following administration.

16. The use of claim 15, wherein the IGF-I SDS is selected from the group consisting of greater than about -1.5 to about 2.0, greater than about -1.0 to about 2.0, greater than about -0.5 to about 2.0, greater than about 0 to about 2.0, greater than about 0.5 to about 2.0, greater than about 1.0 to about 2.0, and greater than about 1.5 to about 2.0.

17. The use of claim 15, wherein the IGF-I SDS is selected from the group consisting of greater than about -1.0 to about 2.0, greater than about 0 to about 2.0, and greater than about 1.0 to about 2.0.

18. The use of claim 15, wherein the pediatric patient exhibits said serum IGF-I SDS following administration of the bolus dose, wherein the administration is once a month, twice a month, three times a month, or four times a month.

19. The use of claim18, wherein the pediatric patient exhibits said serum IGF-I SDS following administration of the bolus dose, wherein the administration is every two weeks, semimonthly, or monthly.

20. The use of claim 19, wherein the pediatric patient exhibits said serum IGF-I SDS following administration of at least a second, or a third, or a fourth bolus dose.

21. The use of claim 15, wherein the bolus dose is effective to maintain the pediatric patient's serum IGF-I SDS between about -2.0 and about 2.0 for at least about 7 days, at least about 14 days, at least about 21 days, at least about 30 days, or at least about one month following administration.

22. The use of claim 15, wherein the bolus dose is effective to maintain the pediatric patient's serum IGF-I SDS between about -2.0 and about 2.0 for at least about 14 days, at least about 21 days, or at least about 30 days following administration.

23. The use of claim 1, wherein the hGH-XTEN fusion protein is prepared for administering to the pediatric patient with PGHD as a therapeutically effective bodyweight adjusted initial bolus dose between about 0.8 mg/kg and about 6.3 mg/kg and a plurality of subsequent bolus doses of the hGH-XTEN fusion protein between about 0.8 mg/kg and about 6.3 mg/kg.

24. The use of claim 22 or claim 23, wherein the IGF-I SDS is maintained between about -2.0 and about 2.0 following administration of a first, or a second, or a third, or a fourth bolus dose.

25. The use of claim 1, wherein the bolus dose is selected from the group consisting of about 0.8 mg/kg, about 1.0 mg/kg, about 1.2 mg/kg, about 1.4 mg/kg, about 1.6 mg/kg, about 1.8 mg/kg, about 2.0 mg/kg, about 2.2 mg/kg, about 2.4 mg/kg, about 2.6 mg/kg, about 2.7 mg/kg, about 2.8 mg/kg, about 3 mg/kg, about 3.2 mg/kg, about 3.4 mg/kg, about 3.6 mg/kg, about 3.8 mg/kg, about 4.0 mg/kg, about 4.2 mg/kg, about 4.4 mg/kg, about 4.6 mg/kg, about 4.8 mg/kg, about 5.0 mg/kg, about 5.2 mg/kg, about 5.4 mg/kg, about 5.6 mg/kg, about 5.8 mg/kg, about 6.0 mg/kg, and about 6.3 mg/kg.

26. The use of claim 1, wherein the bolus dose is about 0.8 mg/kg to about 1.5 mg/kg.

27. The use of claim 1, wherein the bolus dose is about 1.8 mg/kg to about 3.2 mg/kg.

28. The use of claim 1, wherein the bolus dose is about 3.5 mg/kg to about 6.3 mg/kg.

29. The use of claim 1, wherein the hGH-XTEN fusion protein comprises the amino acid sequence of SEQ ID NO:1.

30. The use of claims 1, wherein the hGH-XTEN fusion protein has at least about 91%, or at least about 92%, or at least about 93%, or at least about 94%, or at least about 95%, or at least about 96%, or at least about 97%, or at least about 98%, or at least about 99% sequence identity to SEQ ID NO:1.

31. Use of a human growth hormone-XTEN (hGH-XTEN) fusion protein comprising an amino acid sequence having at least about 90% sequence identity to SEQ ID NO:1 in the manufacture of a medicament for treating human pediatric growth hormone deficiency (PGHD) in a human pediatric patient, wherein the hGH-XTEN fusion protein is prepared for administering to the patient with PGHD as a therapeutically effective bodyweight adjusted bolus dose that is effective to maintain the patient's serum IGF-I standard deviation score (SDS) between about -2.0 and about 2.0 for at least 7 days after administration of the bolus dose.

32. The use of claim 31, wherein the bolus dose is between about 0.8 mg/kg and about 6.3 mg/kg.

34. The use of claim 31, wherein the bolus dose is effective to maintain the pediatric patient's serum IGF-I SDS between about -2.0 and about 2.0 for at least about 14 days, at least about 21 days, or at least about 30 days following administration.

35. The use of claim 31, wherein the bolus dose is effective to maintain the pediatric patient's serum IGF-I SDS between about 0.5 and about 2.0 for at least about 14 days, or at least about 30 days following administration.

36. A pediatric bolus dose of an hGH-XTEN fusion protein comprising an amino acid sequence having at least about 90% sequence identity to SEQ ID NO:1, wherein the bolus dose is a therapeutically effective bodyweight adjusted bolus dose comprising between about 0.8 mg/kg and about 6.3 mg/kg of hGH-XTEN fusion protein.

37. The bolus dose of an hGH-XTEN fusion protein of claim 36 for administering to a pediatric patient with human pediatric growth hormone deficiency (PGHD).

38. The bolus dose of an hGH-XTEN fusion protein of claim 36, wherein the hGH-XTEN fusion protein comprises the amino acid sequence of SEQ ID NO:1.

39. The bolus dose of an hGH-XTEN fusion protein of claim 36, which is formulated for subcutaneous administration.

40. A kit for the treatment of pediatric growth hormone deficiency (PGHD) comprising
(i) a container which holds a pharmaceutical composition comprising a human growth hormone-XTEN (hGH-XTEN) fusion protein comprising an amino acid sequence having at least about 90% sequence identity to SEQ ID NO:1, and
(ii) a package insert associated with said container, wherein the package insert indicates that said composition is for the treatment of pediatric growth hormone deficiency (PGHD) in a pediatric patient by administration of an initial dose of the hGH-XTEN fusion protein between about 0.8 mg/kg and about 6.3 mg/kg and a plurality of subsequent doses of the hGH-XTEN fusion protein between about 0.8 mg/kg and about 6.3 mg/kg, wherein the doses are administered once a month, twice a month, three times a month, or four times a month.

41. The kit of claim 40, wherein the container further comprises a pharmaceutically acceptable carrier.

42. The use of claim 31, wherein the hGH-XTEN fusion protein is prepared for administering to the pediatric patient with PGHD as a therapeutically effective bodyweight adjusted initial bolus dose between about 0.8 mg/kg and about 6.3 mg/kg and

a plurality of subsequent bolus doses of the hGH-XTEN fusion protein between about 0.8 mg/kg and about 6.3 mg/kg.

43. The use of claim 10, wherein the hGH-XTEN fusion protein administered is comparable, on a molar basis, to an equivalent amount of an hGH not linked to XTEN and administered to a pediatric patient.

44. The use of claim 2, wherein the method is effective to maintain the pediatric patient's height velocity within at least about 10%, at least about 20%, or at least about 30% of that compared to the height velocity achieved in pediatric patients administered daily injections of hGH not linked to XTEN of an equivalent amount, on a molar basis, over a comparable dose period.

45. The use of claim 1 or claim 31, wherein the bolus dose of the hGH-XTEN administered provides an area under the curve of about 5.6 Log [AUC (h ng/mL)] to about 7.6 Log [AUC (h ng/mL)].

46. The use of claim 1 or claim 31, wherein the bolus dose of the hGH-XTEN administered provides hGH-XTEN plasma concentration of at least 10 ng/ml.

47. The use of claim 46, wherein the bolus dose of the hGH-XTEN maintains said plasma concetration for at least about 7 days, at least about 14 days or at least about 30 days following administration.