WHAT IS CLAIMED IS:

1. An isolated fusion protein, comprising a growth hormone (GH) that is at least 90% identical to an amino acid sequence selected from Table 1, wherein said growth hormone is linked to an extended recombinant polypeptide (XTEN) of at least 200 amino acids residues, wherein the XTEN is characterized in that:

(a) the XTEN sequence comprises at least 200 contiguous amino acids that exhibits at least 90% sequence identity to a comparable length of an amino acid sequence selected from Table 3;

(b) the XTEN sequence lacks a predicted T-cell epitope when analyzed by TEPITOPE algorithm, wherein the TEPITOPE algorithm prediction for epitopes within the XTEN sequence is based on a score of -6 or greater;

(c) it has a subsequence score of less than 10;

(d) the sum of glycine (G), alanine (A), serine (S), threonine (T), glutamate (E) and proline (P) residues constitutes more than 90% of the total amino acid residues of the XTEN; and

(e) the XTEN sequence is substantially non-repetitive such that (i) at least 80% of the XTEN sequence consists of non-overlapping sequence motifs wherein each of the sequence motifs has 9 to 14 amino acid residues and wherein the sequence of any two contiguous amino acid residues does not occur more than twice in each of the sequence motifs; or (ii) the XTEN sequence contains no three contiguous amino acids that are identical unless the amino acids are serine residues, in which case no more than three contiguous amino acids are serine.

2. The isolated fusion protein of claim 1, wherein the growth hormone is a human growth hormone.

3. The isolated fusion protein of claim 1 or 2, further comprising a second XTEN sequence, and wherein the fusion protein adopts a multiple -XTEN configuration shown in Table 5.

4. The isolated fusion protein of any one of claims 1 to 3, wherein the growth hormone peptide and the XTEN is linked via a spacer, wherein the spacer sequence comprises between 1 to 50 amino acid residues, and wherein the spacer optionally comprises a cleavage sequence.

5. The isolated fusion protein of any of claims 1 to 4, wherein the fusion protein binds to the same target receptor of the corresponding native growth hormone that lacks the XTEN, and wherein said fusion protein retains at least 0.1%-30% of the binding affinity of the corresponding growth hormone that lacks the XTEN.

6. The isolated fusion protein of any of claims 1 to 5, comprising an amino acid sequence that has at least 90% sequence identity to an amino acid sequence selected from Table 35, Table 36, and Table 37.

7. A pharmaceutical composition comprising the isolated fusion protein of any of claims 1 to 6, and a pharmaceutically acceptable carrier.

8. The isolated protein of any of claims 1 to 6 that is configured according to formula I: $(XTEN)_x$-GH-$(XTEN)_y$, (I) wherein independently for each occurrence:

(a) x is either 0 or 1 ; and

(b) y is either 0 or 1, wherein $x+y \geq 1$.

9. The isolated fusion protein of any of claims 1 to 6, wherein the XTEN is fused to the growth hormone on an N- or C-terminus of the growth hormone.

10. The isolated fusion protein of any of claims 1 to 6 and 8 to 9, comprising a human growth hormone of Table 1 and a first and a second XTEN selected from AE912, AM923, AE144, and AE288 of Table 3.

11. The isolated fusion protein of any of claims 1 to 6 and 8 to 10, characterized in that:

(i) it has a longer terminal half- life when administered to a subject compared to the corresponding growth hormone that lacks the XTEN when administered to a subject at a comparable molar dose;

(ii) when a smaller molar amount of the fusion protein is administered to a subject in comparison to the corresponding growth hormone that lacks the XTEN administered to a subject under an otherwise equivalent dose regimen, the fusion protein achieves a comparable area under the curve (AUC) as the corresponding growth hormone that lacks the XTEN;

(iii) when a smaller molar amount of the fusion protein is administered to a subject in comparison to the corresponding growth hormone that lacks the XTEN administered to a subject under an otherwise equivalent dose regimen, the fusion protein achieves a comparable therapeutic effect as the corresponding growth hormone that lacks the XTEN;

(iv) when the fusion protein is administered to a subject less frequently in comparison to the corresponding growth hormone that lacks the XTEN administered to a subject using an otherwise equivalent molar amount, the fusion protein achieves a comparable area under the curve (AUC) as the corresponding growth hormone that lacks the XTEN;

(v) when the fusion protein is administered to a subject less frequently in comparison to the corresponding growth hormone that lacks the XTEN administered to a subject using an otherwise equivalent molar amount, the fusion protein achieves a comparable therapeutic effect as the corresponding growth hormone that lacks the XTEN;

(vi) when an accumulatively smaller molar amount of the fusion protein is administered to a subject in comparison to the corresponding growth hormone that lacks the XTEN administered to a

subject under an otherwise equivalent dose period, the fusion protein achieves comparable area under the curve (AUC) as the corresponding growth hormone that lacks the XTEN; or

(vii) when an accumulatively smaller molar amount of the fusion protein is administered to a subject in comparison to the corresponding growth hormone that lacks the XTEN administered to a subject under an otherwise equivalent dose period, the fusion protein achieves comparable therapeutic effect as the corresponding growth hormone that lacks the XTEN.

12. A method of producing a fusion protein comprising a growth hormone (GH) fused to one or more extended recombinant polypeptides (XTEN), comprising:

(a) providing host cell comprising a recombinant polynucleotide molecule encoding the fusion protein of claim 1 or 6;

(b) culturing the host cell under conditions permitting the expression of the fusion protein; and

(c) recovering the fusion protein.

13. The method of claim 12, wherein the growth hormone of the fusion protein has at least 90% sequence identity to:

(a) a human growth hormone; or

(b) the human growth hormone sequence selected from Table 1.

14. The method of claim 12 or 13, wherein the one or more XTEN of the expressed fusion protein has at least 90% sequence identity to a sequence selected from Table 3.

15. The method of any of claims 12 to 14, wherein the polynucleotide molecule encoding the fusion protein comprises a nucleic acid sequence exhibiting at least 90% sequence identity of a nucleic acid sequence selected from Table 35, Table 36, and Table 37.

16. The method of any of claims 12 to 15, wherein the polynucleotide is codon optimized for enhanced expression of said fusion protein in the host cell.

17. The method any of claims 12 to 16, wherein the host cell is a prokaryotic cell.

18. The method of any of claims 12 to 17, wherein the isolated fusion protein is recovered from the host cell cytoplasm in substantially soluble form.

19. An isolated nucleic acid comprising a nucleotide sequence encoding the fusion protein of any of claims 1 to 6 and 8 to 11 or the complement thereof.

20. An expression vector comprising the nucleic acid of claim 19.

21. An isolated host cell comprising the nucleic acid of claim 19.

22. A fusion protein comprising a growth hormone (GH) for treating a growth-hormone related condition in a subject, comprising the fusion protein of any of claims 1 to 6 and 8 to 11.

23. The fusion protein of claim 22, wherein the growth-hormone related condition is selected from growth-hormone deficiency, Turner's Syndrome, Prader-Willi Syndrome, idiopathic short stature, AIDS wasting, multiple sclerosis, Crohn's disease, ulcerative colitis, and muscular dystrophy.

24. The fusion protein of claim 22 or 23, wherein a therapeutically effective amount of the fusion protein results in maintaining blood concentrations of the fusion protein within a therapeutic window for the fusion protein at least three-fold longer compared to the corresponding native growth hormone that lacks the XTEN administered at a comparable amount to a subject.

25. The fusion protein of any of claims 22 to 24, wherein two or more consecutive doses of the fusion protein administered under a therapeutically effective dose regimen results in a gain in time between consecutive C_{max} peaks and/or C_{mn} troughs for blood levels of the fusion protein compared to the corresponding growth hormone not linked to the fusion protein and administered using a therapeutically dose regimen established for the GH.

26. The fusion protein of any of claims 22 to 25, wherein

(i) a smaller molar amount of the fusion protein in comparison to the corresponding growth hormone that lacks the XTEN achieves a comparable therapeutic effect as the corresponding growth hormone that lacks the XTEN;

(ii) the fusion protein is administered less frequently to a subject in comparison to the corresponding growth hormone that lacks the XTEN administered to a subject using an otherwise equivalent molar dose, and the fusion protein achieves a comparable therapeutic effect as the corresponding growth hormone that lacks the XTEN; or

(iii) an accumulatively smaller molar amount of the fusion protein is administered to a subject in comparison to the corresponding growth hormone that lacks the XTEN administered to a subject under the otherwise equivalent dose period, the fusion protein achieves a comparable therapeutic effect as the corresponding growth hormone that lacks the XTEN.

27. The fusion protein of claim 26, wherein the therapeutic effect is a measured parameter selected from IGF- 1 concentrations, IGFBP3 concentration, height velocity, lean body mass, total body fat, trunk fat, response to insulin challenge, rate of division of chondrocytes, chondrocyte numbers, bone density, bone growth, and increase in epiphyseal plate width.

28. A kit, comprising the pharmaceutical composition of claim 7, a label identifying the pharmaceutical composition, and an instruction for storage, reconstitution and/or administration of the pharmaceutical compositions to a subject.

29. A fusion protein, comprising an amino acid sequence that is at least 90% identical to the amino acid sequence of AE912-hGH-AE144 as shown in Table 36.

30. The fusion protein of claim 29, comprising an amino acid sequence that is at least 95% identical to the amino acid sequence of AE912-hGH-AE144 as shown in Table 36.

31. The fusion protein of claim 29, comprising an amino acid sequence that is at least 99% identical to the amino acid sequence of AE912-hGH-AE144 as shown in Table 36.

32. A fusion protein, comprising the amino acid sequence of AE912-hGH-AE144 as shown in Table 36.

33. An isolated nucleic acid comprising a nucleotide sequence encoding the fusion protein of any one of claims 29-32, or the complement thereof.

34. An expression vector comprising the nucleic acid of claim 33.

35. An isolated host cell comprising the nucleic acid of claim 33.

36. The isolated host cell of claim 21 or claim 35, wherein the host cell is a prokaryotic host cell.

37. Use of a therapeutically effective amount of a fusion protein of any one of claims 29-32, in the manufacture of a medicament for treating a growth-hormone related condition in a subject.

38. The use of claim 37, wherein the growth-hormone related condition is selected from growth-hormone deficiency, Turner's Syndrome, Prader-Willi Syndrome, idiopathic short stature, AIDS wasting, multiple sclerosis, Crohn's disease, ulcerative colitis, and muscular dystrophy.

39. A pharmaceutical composition comprising the isolated fusion protein of any one of claims 29-32, and a pharmaceutically acceptable carrier.

40. A kit, comprising the pharmaceutical composition of claim 39, a label identifying the pharmaceutical composition, and an instruction for storage, reconstitution and/or administration of the pharmaceutical compositions to a subject.

41. The fusion protein of claim 1 or 2, further comprising an additional XTEN polypeptide sequence having at least 90% sequence identity to the amino acid sequence of amino acids 1106 to 1251 of AE912-hGH-AE144 as shown in Table 36.

42. The fusion protein of claim 41, wherein the additional XTEN polypeptide sequence has at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity to the sequence of amino acids 1106 to 1251 of AE912-hGH-AE144 as shown in Table 36.

43. The fusion protein of claim 41, wherein the additional XTEN polypeptide sequence has at least 98% or 99% identity to the sequence of amino acids 1106 to 1251 of AE912-hGH-AE144 as shown in Table 36.

44. The fusion protein of claim 41, wherein the additional XTEN polypeptide sequence comprises the sequence of amino acids 1106 to 1251 of AE912-hGH-AE144 as shown in Table 36.

WHAT IS CLAIMED IS:

1. An isolated fusion protein, comprising a growth hormone (GH) that is at least 90% identical to an amino acid sequence selected from Table 1 , wherein said growth hormone is linked to an extended recombinant polypeptide (XTEN) of at least 200 amino acids residues, wherein the XTEN is characterized in that:

(a) the XTEN sequence comprises at least 200 contiguous amino acids that exhibits at least 90% sequence identity to a comparable length of an amino acid sequence selected from Table 3;

(b) the XTEN sequence lacks a predicted T-cell epitope when analyzed by TEPITOPE algorithm, wherein the TEPITOPE algorithm prediction for epitopes within the XTEN sequence is based on a score of -9 or greater;

(c) it has a subsequence score of less than 10; and

(d) the sum of glycine (G), alanine (A), serine (S), threonine (T), glutamate (E) and proline (P) residues constitutes more than 90% of the total amino acid residues of the XTEN.

(e) the XTEN sequence is substantially non-repetitive such that (i) at least 80% of the XTEN sequence consists of non-overlapping sequence motifs wherein each of the sequence motifs has at least 9 to 14 amino acid residues and wherein the sequence of any two contiguous amino acid residues does not occur more than twice in each of the sequence motifs; or (ii) the XTEN sequence contains no three contiguous amino acids that are identical unless the amino acids are serine residues.

2. The isolated fusion protein of claim 1 , wherein the growth hormone is a human growth hormone.

3. The isolated fusion protein of claim 1 or 2, further comprising a second XTEN sequence, and wherein the fusion protein adopts a multiple -XTEN configuration shown in Table 5.

4. The isolated fusion protein of any one of claims 1 to 3, wherein the growth hormone peptide and the XTEN is linked via a spacer, wherein the spacer sequence comprises between 1 to 50 amino acid residues, and wherein the spacer optionally comprises a cleavage sequence.

5. The isolated fusion protein of any of claims 1 to 4, wherein the fusion protein binds to the same target receptor of the corresponding native growth hormone that lacks the XTEN, and wherein said fusion protein retains at least 0.1%-30% of the binding affinity of the corresponding growth hormone that lacks the XTEN.

6. The isolated fusion protein of any of claims 1 to 5, comprising an amino acid sequence that has at least 90% sequence identity to an amino acid sequence selected from Table 35, Table 36, and Table 37.

7. A pharmaceutical composition comprising the isolated fusion protein of any of claims 1 to 6, and a pharmaceutically acceptable carrier.

8. The isolated protein of any of claims 1 to 6 that is configured according to formula I: $(XTEN)_x$-GH-$(XTEN)_5$, (I) wherein independently for each occurrence:

(a) x is either 0 or 1 ; and

(b) y is either 0 or 1, wherein x+y>1.

9. The isolated fusion protein of any of claims 1 to 6, wherein the XTEN is fused to the growth hormone on an N- or C-terminus of the growth hormone.

10. The isolated fusion protein of any of claims 1 to 6 and 8 to 9, comprising a human growth hormone of Table 1 and a first and a second XTEN selected from AE912, AM923, AE144, and AE288 of Table 3.

11. The isolated fusion protein of any of claims 1 to 6 and 8 to 10, characterized in that:

(i) it has a longer terminal half- life when administered to a subject compared to the corresponding growth hormone that lacks the XTEN when administered to a subject at a comparable molar dose;

(ii) when a smaller molar amount of the fusion protein is administered to a subject in comparison to the corresponding growth hormone that lacks the XTEN administered to a subject under an otherwise equivalent dose regimen, the fusion protein achieves a comparable area under the curve (AUC) as the corresponding growth hormone that lacks the XTEN;

(iii) when a smaller molar amount of the fusion protein is administered to a subject in comparison to the corresponding growth hormone that lacks the XTEN administered to a subject under an otherwise equivalent dose regimen, the fusion protein achieves a comparable therapeutic effect as the corresponding growth hormone that lacks the XTEN;

(iv) when the fusion protein is administered to a subject less frequently in comparison to the corresponding growth hormone that lacks the XTEN administered to a subject using an otherwise equivalent molar amount, the fusion protein achieves a comparable area under the curve (AUC) as the corresponding growth hormone that lacks the XTEN;

(v) when the fusion protein is administered to a subject less frequently in comparison to the corresponding growth hormone that lacks the XTEN administered to a subject using an otherwise equivalent molar amount, the fusion protein achieves a comparable therapeutic effect as the corresponding growth hormone that lacks the XTEN;

(vi) when an accumulatively smaller molar amount of the fusion protein is administered to a subject in comparison to the corresponding growth hormone that lacks the XTEN administered to a subject under an otherwise equivalent dose period, the fusion protein achieves comparable area under the curve (AUC) as the corresponding growth hormone that lacks the XTEN; or

(vii) when an accumulatively smaller molar amount of the fusion protein is administered to a subject in comparison to the corresponding growth hormone that lacks the XTEN administered to a subject under an otherwise equivalent dose period, the fusion protein achieves comparable therapeutic effect as the corresponding growth hormone that lacks the XTEN.

12. A method of producing a fusion protein comprising a growth hormone (GH) fused to one or more extended recombinant polypeptides (XTEN), comprising:

(a) providing host cell comprising a recombinant polynucleotide molecule encoding the fusion protein of claim 1 or 6;

(b) culturing the host cell under conditions permitting the expression of the fusion protein; and

(c) recovering the fusion protein.

13. The method of claim 12, wherein the growth hormone of the fusion protein has at least 90% sequence identity to:

(a) a human growth hormone; or

(b) the human growth hormone sequence selected from Table 1.

14. The method of claim 12 or 13, wherein the one or more XTEN of the expressed fusion protein has at least 90% sequence identity to a sequence selected from Table 3.

15. The method of any of claims 12 to 14, wherein the polynucleotide molecule encoding the fusion protein comprises a nucleic acid sequence exhibiting at least 90% sequence identity of a nucleic acid sequence selected from Table 35, Table 36, and Table 37.

16. The method of any of claims 12 to 15, wherein the polynucleotide is codon optimized for enhanced expression of said fusion protein in the host cell.

17. The method any of claims 12 to 16, wherein the host cell is a prokaryotic cell.

18. The method of any of claims 12 to 17, wherein the isolated fusion protein is recovered from the host cell cytoplasm in substantially soluble form.

19. An isolated nucleic acid comprising a nucleotide sequence encoding the fusion protein of any of claims 1 to 6 and 8 to 11 or the complement thereof.

20. An expression vector comprising the nucleic acid of claim 19.

21. An isolated host cell comprising the nucleic acid of claim 19.

22. A fusion protein comprising a growth hormone (GH)for treating a growth-hormone related condition in a subject, comprising the fusion protein of any of claims 1 to 6 and 8 to 11.

23. The fusion protein of claim 22, wherein the growth-hormone related condition is selected from growth-hormone deficiency, Turner's Syndrome, Prader-Willi Syndrome, idiopathic short stature, AIDS wasting, multiple sclerosis, Crohn's disease, ulcerative colitis, and muscular dystrophy.

24. The fusion protein of claim 22 or 23, wherein a therapeutically effective amount of the fusion protein results in maintaining blood concentrations of the fusion protein within a therapeutic window for the fusion protein at least three-fold longer compared to the corresponding native growth hormone that lacks the XTEN administered at a comparable amount to a subject.

25. The fusion protein of any of claims 22 to 24, wherein two or more consecutive doses of the fusion protein administered under a therapeutically effective dose regimen results in a gain in time between consecutive C_{max} peaks and/or C_{mn} troughs for blood levels of the fusion protein compared to the corresponding growth hormone not linked to the fusion protein and administered using a therapeutically dose regimen established for the GH.

26. The fusion protein of any of claims 22 to 25, wherein

(i) a smaller molar amount of the fusion protein in comparison to the corresponding growth hormone that lacks the XTEN achieves a comparable therapeutic effect as the corresponding growth hormone that lacks the XTEN;

(ii) the fusion protein is administered less frequently to a subject in comparison to the corresponding growth hormone that lacks the XTEN administered to a subject using an otherwise equivalent molar dose, and the fusion protein achieves a comparable therapeutic effect as the corresponding growth hormone that lacks the XTEN; or

(iii) an accumulatively smaller molar amount of the fusion protein is administered to a subject in comparison to the corresponding growth hormone that lacks the XTEN administered to a subject under the otherwise equivalent dose period, the fusion protein achieves a comparable therapeutic effect as the corresponding growth hormone that lacks the XTEN.

27. The fusion proteinof claim 26, wherein the therapeutic effect is a measured parameter selected from IGF- 1 concentrations, IGFBP3 concentration, height velocity, lean body mass, total body fat, trunk fat, response to insulin challenge, rate of division of chondrocytes, chondrocyte numbers, bone density, bone growth, and increase in epiphyseal plate width.

28. A kit, comprising the pharmaceutical composition of claim 7, a label identifying the pharmaceutical composition, and an instruction for storage, reconstitution and/or administration of the pharmaceutical compositions to a subject.

29. A fusion protein, comprising an amino acid sequence that is at least 90% identical to the amino acid sequence of AE912-hGH-AE144 as shown in Table 36.

30. The fusion protein of claim 29, comprising an amino acid sequence that is at least 95% identical to the amino acid sequence of AE912-hGH-AE144 as shown in Table 36.

31. The fusion protein of claim 29, comprising an amino acid sequence that is at least 99% identical to the amino acid sequence of AE912-hGH-AE144 as shown in Table 36.

32. A fusion protein, comprising the amino acid sequence of AE912-hGH-AE144 as shown in Table 36.

33. An isolated nucleic acid comprising a nucleotide sequence encoding the fusion protein of any one of claims 29-32, or the complement thereof.

34. An expression vector comprising the nucleic acid of claim 33.

35. An isolated host cell comprising the nucleic acid of claim 33.

36. The isolated host cell of claim 21 or claim 35, wherein the host cell is a prokaryotic host cell.

37. Use of a therapeutically effective amount of a fusion protein of any one of claims 29-32, in the manufacture of a medicament for treating a growth-hormone related condition in a subject.

38. The use of claim 37, wherein the growth-hormone related condition is selected from growth-hormone deficiency, Turner's Syndrome, Prader-Willi Syndrome, idiopathic short stature, AIDS wasting, multiple sclerosis, Crohn's disease, ulcerative colitis, and muscular dystrophy.

39. A pharmaceutical composition comprising the isolated fusion protein of any one of claims 29-32, and a pharmaceutically acceptable carrier.

40. A kit, comprising the pharmaceutical composition of claim 39, a label identifying the pharmaceutical composition, and an instruction for storage, reconstitution and/or administration of the pharmaceutical compositions to a subject.

41. The fusion protein of claim 1 or 2, further comprising an additional XTEN polypeptide sequence having at least 90% sequence identity to the amino acid sequence of amino acids 1106 to 1251 of AE912-hGH-AE144 as shown in Table 36.

42. The fusion protein of claim 41, wherein the additional XTEN polypeptide sequence has at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity to the sequence of amino acids 1106 to 1251 of AE912-hGH-AE144 as shown in Table 36.

43. The fusion protein of claim 41, wherein the additional XTEN polypeptide sequence has at least 98% or 99% identity to the sequence of amino acids 1106 to 1251 of AE912-hGH-AE144 as shown in Table 36.

44. The fusion protein of claim 41, wherein the additional XTEN polypeptide sequence comprises the sequence of amino acids 1106 to 1251 of AE912-hGH-AE144 as shown in Table 36.