CLAIMS

1. Use of an extended release composition comprising:

   a. an organic solvent;

   b. 40 mg to 50 mg of leuprolide, or a pharmaceutically acceptable salt thereof; and

   c. a biodegradable polymer comprising polymer segments selected from 85:15 poly(lactide-co-glycolide) (PLG) copolymer segments, 85:15 poly(lactic acid-co-glycolic acid) (PLGA) copolymer segments, poly(lactide) (PL) polymer segments, poly(lactic acid) (PLA) polymer segments, or combinations thereof, wherein the polymer has substantially no titratable carboxylic acid groups and wherein at least one distal end group of the polymer is hydroxyl-terminated;

in the manufacture of a medicament for the treatment of central precocious puberty in a child of at least 2 years of age by subcutaneous administration of the extended release composition once every six months, wherein:

the amount of leuprolide, or a pharmaceutically acceptable salt thereof, administered to the child is independent from the weight of the child and is not modified in subsequent administrations of the extended release composition;

upon contact of the extended release composition with a bodily fluid, the solvent dissipates and an *in situ* solid depot forms; and

the extended release composition reduces the child's peak stimulated blood serum LH concentration to a pre-pubertal concentration level of <4 IU/L when administered once every six months.

2. Use of a product, comprising:

   a. an extended release composition, comprising:

      i. an organic solvent;

      ii. 40 mg to 50 mg of leuprolide, or a pharmaceutically acceptable salt thereof; and

      iii. a biodegradable polymer comprising polymer segments selected from 85:15 poly(lactide-co-glycolide) (PLG) copolymer segments, 85:15 poly(lactic acid-co-glycolic acid) (PLGA) copolymer segments, poly(lactide) (PL) polymer segments, poly(lactic acid) (PLA) polymer

segments, or a combination thereof, wherein the polymer has substantially no titratable carboxylic acid groups and wherein at least one distal end group of the polymer is hydroxyl-terminated; and

b. a stimulation composition comprising GnRH or a GnRH agonist, or a pharmaceutically acceptable salt thereof;

in the manufacture of a medicament for the treatment of central precocious puberty in a child of at least 2 years of age, wherein:

the extended release composition is formulated for subcutaneous injection once every six months and the stimulation composition is formulated for injection three to six months after the extended release composition;

the amount of leuprolide, or a pharmaceutically acceptable salt thereof, in the extended release composition is independent from the weight of the child and is not modified in subsequent administrations of the extended release composition;

upon contact of the extended release composition with a bodily fluid, the solvent dissipates and an *in situ* solid depot forms;

the extended release composition reduces the child's peak stimulated blood serum LH concentration to a pre-pubertal concentration level of <4 IU/L when administered once every six months; and

the stimulation composition confirms suppression of blood serum LH concentration to pre-pubertal level of <4 IU/L.

3. Use according to claim 1 or claim 2, wherein the leuprolide or pharmaceutically acceptable salt thereof is leuprolide acetate and the amount of leuprolide acetate in the extended release composition is 45 mg.

4. Use according to claim 1 or claim 2, wherein the amount of leuprolide or the pharmaceutically acceptable salt thereof in the extended release composition is selected from: 40 mg – 45 mg leuprolide free base equivalent, and 42 mg leuprolide free base equivalent.

5. Use according to claim 2, wherein the stimulation composition comprises at least one GnRH agonist or pharmaceutically acceptable salt thereof selected from the

group consisting of leuprolide, gonadorelin, goserelin, histrelin, nafarelin, buserelin, and triptorelin.

6. Use according to claim 2, wherein the stimulation composition comprises one of:

a GnRH solution and is formulated for subcutaneous administration at a dose selected from: a dose of 2.5 µg per kg of body weight and a total dose of 100 µg;

a leuprolide acetate solution formulated for subcutaneous administration at a dose selected from: a dose of 10 µg – 20 µg per kg of body weight and a total dose of 500 µg – 1000 µg;

a nafarelin acetate solution formulated for subcutaneous administration at a dose selected from: a dose of 1 µg per kg of body weight and a total dose of 100 µg;

a buserelin solution formulated for subcutaneous administration at a total dose of 100 µg; and

a triptorelin acetate solution formulated for subcutaneous administration at a total dose of 100 µg.

7. Use according to any one of claims 1-6, wherein the extended release composition:

reduces a peak stimulated blood serum FSH to a concentration of ≤2.5 IU/L;

reduces a peak stimulated blood serum estradiol in a female to a concentration of <73.4 pmol/L (<20 pg/mL); and/or

reduces a peak stimulated blood serum testosterone in a male to a concentration of <1 nmol/L (<28.8 ng/dL).

8. Use according to any one of claims 1-7, wherein the extended release composition comprises:

a. about 165 mg of N-methyl-2-pyrrolidone (NMP);

b. about 45 mg of leuprolide acetate; and

c. about 165 mg of about 85:15 poly(DL lactide-co-glycolide) (PLG) copolymer segment.

9. Use according to any one of claims 1-8, wherein the biodegradable polymer has a weight average molecular weight from 15 kDa – 45 kDa.

10. Use according to any one of claims 1-9, wherein the biodegradable polymer has a weight average molecular weight from 20 kDa – 26 kDa.

11. Use according to any one of claims 1-10, wherein the biodegradable polymer comprises a polymer of the Formula:

HO—(P)—C(=O)O—Ra—O(O=)C—(P)—OH

wherein Ra is an alkane diradical comprising about 4 – about 8 carbons and is a residue of an alkane diol; and

wherein each P is independently a polymeric and/or copolymer segment.

12. Use according to any one of claims 1-11, wherein the extended release composition:

reduces a mean bone growth velocity by 25% over about a twelve-month treatment period; and/or

reduces a mean ratio of bone age to chronological age at the time of measurement by 5% at the end of treatment.

13. Use according to any one of claims 1-12, wherein the extended release composition comprises an injection dose volume selected from 0.375 mL and 0.5 mL or less.

14. Use according to any one of claims 1-7 and 9-13, wherein the organic solvent is NMP.

15. Use according to any one of claims 1-14, wherein the extended release composition is administered for a time period of about 6 months, about 12 months, about 18 months, about 24 months or longer.

16. An extended release composition comprising:

a. an organic solvent;

b. 40 mg to 50 mg of leuprolide, or a pharmaceutically acceptable salt thereof; and

c. a biodegradable polymer comprising polymer segments selected from 85:15 poly(lactide-co-glycolide) (PLG) copolymer segments, 85:15 poly(lactic acid-co-glycolic acid) (PLGA) copolymer segments, poly(lactide) (PL) polymer segments, poly(lactic acid) (PLA) polymer segments, or combinations thereof, wherein the polymer has substantially no titratable carboxylic acid groups and wherein at least one distal end group of the polymer is hydroxyl-terminated;

for use in the treatment of central precocious puberty in a child of at least 2 years of age, wherein:

the extended release composition is formulated for subcutaneous injection once every six months;

the amount of leuprolide, or a pharmaceutically acceptable salt thereof, in the extended release composition is independent from the weight of the child and is not modified in subsequent administrations of the extended release composition;

upon contact of the extended release composition with a bodily fluid, the solvent dissipates and an *in situ* solid depot forms; and

the extended release composition reduces the child's peak stimulated blood serum LH concentration to a pre-pubertal concentration level of <4 IU/L when administered once every six months.

17. The extended release composition of claim 16, wherein the leuprolide or pharmaceutically acceptable salt thereof is leuprolide acetate and the amount of leuprolide acetate in the extended release composition is about 45 mg.

18. The extended release composition of claim 16 or claim 17, wherein the extended release composition:

reduces a peak stimulated blood serum FSH to a concentration of ≤2.5 IU/L;

reduces a peak stimulated blood serum estradiol in a female to a concentration of <73.4 pmol/L (<20 pg/mL); and/or

reduces a peak stimulated blood serum testosterone in a male to a concentration of <1 nmol/L (<28.8 ng/dL).

19. The extended release composition of any one of claims 16-18, wherein the extended release composition comprises:

a. about 165 mg of N-methyl-2-pyrrolidone (NMP);

b. about 45 mg of leuprolide acetate; and

c. about 165 mg of about 85:15 poly(DL lactide-co-glycolide) (PLG) copolymer segment.

20. The extended release composition of any one of claims 16-19, wherein the biodegradable polymer has a weight average molecular weight selected from 15 kDa – 45 kDa.

21. The extended release composition of any one of claims 16-19, wherein the biodegradable polymer has a weight average molecular weight from 20 kDa - 26kDa.

22. The extended release composition of any one of claims 16-20, wherein the extended release composition:

reduces a mean bone growth velocity by about 25% over about a twelve-month treatment period; and/or

reduces a mean ratio of bone age to chronological age at the time of measurement by about 5% at the end of treatment.

23. A kit comprising:

a. at least one dose of an injectable stimulation composition comprising a solution of GnRH or a GnRH agonist, or a pharmaceutically acceptable salt thereof, effective for measuring the peak stimulated blood serum LH concentration within a child of at least 2 years of age who has central precocious puberty (CPP);

b. at least one dose of an injectable extended release composition effective for the treatment of CPP in the child by reducing the peak stimulated blood

serum LH concentration to a pre-pubertal concentration level of <4 IU/L when administered about once every six months and comprising:

i. N-methyl-2-pyrrolidone (NMP);

ii. 40 mg to 50 mg of leuprolide acetate or an equivalent amount of a different pharmaceutically acceptable salt of leuprolide;

iii. a biodegradable polymer comprising polymer segments selected from 85/15 poly(lactide-co-glycolide) (PLG) copolymer segments, 85/15 poly(lactic acid-co-glycolic acid) (PLGA) copolymer segments, poly(lactide) (PL) polymer segments, poly(lactic acid) (PLA) polymer segments, or a combination thereof, wherein the polymer has substantially no titratable carboxylic acid groups and wherein at least one distal end group of the polymer is hydroxyl-terminated;

wherein upon contact of the extended release composition with a bodily fluid, NMP dissipates and an *in situ* solid depot forms; and

c. instructions for the use thereof for treating CPP in the child.