toxin, a botulinum toxin complex, or a reduced botulinum toxin complex component and a positively charged carrier component comprising a positively charged polylysine backbone having covalently attached thereto one or more positively charged efficiency groups having an amino acid sequence of (gly)p-RGRDDRRQRRR-(gly)q, (gly)p-YGRKKRRQRRR-(gly)q or (gly)p-RKKRRQRRR-(gly)q, wherein the subscripts p and q are each independently an integer of from 0 to 20; wherein the botulinum toxin, botulinum toxin complex, or reduced botulinum toxin complex component is administered to the individual in a treatment dose of 20 U to 60 U; wherein the positively charged carrier is non-covalently associated with the botulinum toxin, botulinum toxin complex, or reduced botulinum toxin complex component; and a pharmaceutically acceptable diluent suitable for injection; and wherein the first treatment dose of the composition administered by injection to the individual achieves the extended duration therapeutic or cosmetic effect having at least about a 6 month to about a 10 month duration of effect, optionally, before a second or subsequent treatment dose is administered.

[0021a] In another aspect, the disclosure provides use of botulinum toxin in the manufacture of a sterile injectable composition for achieving an extended duration cosmetic effect in an individual, wherein a treatment dose of the sterile injectable composition is to be administered by injection into an area of the individual in need of treatment to achieve the cosmetic effect following a treatment with the composition; wherein the composition comprises a pharmaceutically acceptable diluent suitable for injection; and a botulinum toxin of serotype A having a molecular weight of 150 kDa; and a positively charged carrier has the amino acid sequence RKKRRQRRRG-$(K)_{15}$-GRKKRRQRRR; wherein the botulinum toxin component is to be administered to the individual in a treatment dose of 40 U; wherein the positively charged carrier is non-covalently associated with the botulinum toxin component; and wherein the treatment dose of the composition administered by injection to the individual achieves the extended duration cosmetic effect having at least a 6 month duration of effect, wherein the cosmetic effect is a reduction in the appearance of glabellar lines.

[0022] In another example, the disclosure provides a method of reducing wrinkles, lines, or furrows in an individual in need thereof, the method comprising administering to the individual as a single dose injection a composition comprising: a botulinum toxin, a botulinum toxin complex, or a reduced botulinum toxin complex and a positively charged carrier comprising a positively charged polylysine backbone having covalently attached thereto one or more positively charged efficiency groups having an amino acid sequence of (gly)p-RGRDDRRQRRR-(gly)q, (gly)p-YGRKKRRQRRR-(gly)q or (gly)p-RKKRRQRRR-(gly)q, wherein the subscripts p and q are each independently an integer of from 0 to 20; and a pharmaceutically acceptable diluent for injection; wherein the botulinum toxin is administered to the individual in an amount of 20 U to 60 U; wherein the positively charged carrier is non-covalently associated with the botulinum toxin, botulinum toxin complex, or reduced botulinum toxin complex component; and wherein the single dose injection of the composition provides a single treatment having at least about a six month to about a 10 month duration of effect in reducing the wrinkles, lines, or furrows in the individual, thereby extending treatment interval duration for the individual. In an example, the composition reduces, or reduces the severity of, glabellar lines in the face of the individual.

[0022a] In one aspect, the disclosure provides a method of reducing wrinkles, lines, or furrows in a glabellar region of an individual in need thereof, the method comprising: administering to the individual a composition comprising: a pharmaceutically acceptable diluent for injection; a botulinum toxin componenst of serotype A having a molecular weight of 150 kDa; and a positively charged carrier has the amino acid sequence RKKRRQRRRG-$(K)_{15}$-GRKKRRQRRR; wherein the botulinum toxin is administered to the individual in an amount of 40 U; wherein the positively charged carrier is non-covalently associated with the botulinum component; and wherein the administration of the composition provides at least a six month duration of effect in reducing the wrinkles, lines, or furrows in the individual.

[0023] In another example, the disclosure provides a sterile injectable composition comprising a botulinum toxin, a botulinum toxin complex, or a reduced botulinum toxin complex

in a dosage amount selected from 20 U, 40 U, or 60 U; and a positively charged carrier comprising a positively charged polylysine backbone having covalently attached thereto one or more positively charged efficiency groups having an amino acid sequence of (gly)p-RGRDDRRQRRR-(gly)q, (gly)p-YGRKKRRQRRR-(gly)q or (gly)p-RKKRRQRRR-(gly)q, wherein the subscripts p and q are each independently an integer of from 0 to 20; and a pharmaceutically acceptable diluent for injection; wherein the positively charged carrier is non-covalently associated with the botulinum toxin, botulinum toxin complex, or reduced botulinum toxin complex component; and wherein the composition provides a cosmetic or therapeutic effect which endures for at least 20 to 24 weeks, or for at least 6 months, or greater than 6 months, e.g., about 6 months to about 10 months, following a treatment of an individual with an effective dose of the injectable composition.

[0023a] In one aspect, the disclosure provides a sterile injectable composition comprising: a botulinum toxin of serotype A having a molecular weight of 150 kDa, in a dosage amount selected from 40 U; and a positively charged carrier has the amino acid sequence RKKRRQRRRG-(K)15-GRKKRRQRRR; and a pharmaceutically acceptable diluent for injection; wherein the positively charged carrier is non-covalently associated with the botulinum toxin component; and wherein the composition provides a cosmetic effect of reducing the appearance of glabellar lines which endures for at least 20 to 24 weeks following a single treatment of an individual with the injectable composition.

[0024] In some examples of these above methods and composition, the composition comprises botulinum toxin of serotype A, preferably a serotype A botulinum toxin having a molecular weight of 150 kDa. In an example, the positively charged carrier has the amino acid sequence RKKRRQRRRG-$(K)_{15}$-GRKKRRQRRR. In an example, the botulinum toxin is present in the composition in a dosage amount of 20 U. In an example, the botulinum toxin is present in the composition in a dosage amount of 40 U. In an example, the botulinum toxin is present in the composition in a dosage amount of 60 U. In an example, the composition reduces the severity of glabellar lines in an individual who has undergone a single treatment by injection of the composition. In certain examples, the duration of the treatment effect comprises greater than 6 months; greater than 7 months; greater than 8 months; greater than 9 months; or at least 6 months through 10 months.

[0025] In another of its examples, the disclosure provides a method of treating an individual who is in need of treatment with injectable botulinum toxin, in which the method of treatment comprises a treatment course having multiple treatment intervals with prolonged duration of effect and duration time between each treatment interval, the treatment course comprising: administering by injection an initial treatment dose of a sterile injectable composition into an area of the individual in need of treatment to achieve a therapeutic or a cosmetic effect following the initial treatment with the composition; wherein the composition comprises a botulinum toxin, a botulinum toxin complex, or a reduced botulinum toxin complex component and a positively charged carrier component comprising a positively charged polylysine backbone having

covalently attached thereto one or more positively charged efficiency groups having an amino acid sequence of (gly)p-RGRDDRRQRRR-(gly)q, (gly)p-YGRKKRRQRRR-(gly)q or (gly)p-RKKRRQRRR-(gly)q, wherein the subscripts p and q are each independently an integer of from 0 to 20; and a pharmaceutically acceptable diluent suitable for injection; wherein the botulinum toxin, botulinum toxin complex, or reduced botulinum toxin complex component is administered to the individual in a treatment dose of 20 U to 60 U; wherein the positively charged carrier is non-covalently associated with the botulinum toxin, botulinum toxin complex, or reduced botulinum toxin complex component; wherein the initial treatment dose of the composition administered by injection to the individual provides a therapeutic or cosmetic duration of effect lasting through at least about 10 months; and administering subsequent treatment doses of the composition by injection to the individual at treatment intervals comprising a duration of greater than or equal to 3 months to at least about 10 months following the initial treatment dose and between each subsequent treatment dose.

[0025a] In one aspect, the disclosure provides a method of treating an individual in need of treatment with injectable botulinum toxin, wherein the method of treatment comprises a treatment course having multiple treatment intervals with prolonged duration of effect and duration time between each treatment interval, the treatment course comprising: administering by injection an initial treatment dose of a sterile injectable composition into an area of the individual in need of treatment to achieve a cosmetic effect following the initial treatment with the composition; wherein the composition comprises a pharmaceutically acceptable diluent suitable for injection; a botulinum toxin of serotype A having a molecular weight of 150 kDa; and a positively charged carrier has the amino acid sequence RKKRRQRRRG-$(K)_{15}$-GRKKRRQRRR; and wherein the botulinum toxin component is administered to the individual in a treatment dose of 40 U; wherein the positively charged carrier is non-covalently associated with the botulinum toxin component; wherein the initial treatment dose of the composition administered by injection to the individual provides a cosmetic effect lasting through at least 6 months, wherein the cosmetic effect is reducing the appearance of glabellar lines; and administering subsequent treatment doses of the composition by injection to the individual at treatment intervals comprising a duration of greater than or equal to 6 months to at least 9 months following the initial treatment dose and between each subsequent treatment dose.

[0026] In examples of the above-described treatment method, the therapeutic or cosmetic effect is treatment or reduction of wrinkles, lines, or furrows. In an example, the therapeutic or cosmetic effect is reduction of glabellar lines in the face of the individual. In an example, the composition comprises botulinum toxin of serotype A, preferably, botulinum toxin of serotype A having a molecular weight of 150 kDa. In an example, the positively charged carrier is a positively charged peptide having the amino acid sequence RKKRRQRRRG-(K)15-GRKKRRQRRR. In an example, the composition does not locally diffuse from the site of injection following injection. In specific examples, the botulinum toxin is administered to the individual in an amount of 20 U, or in an amount of 40 U, or in an amount of 60 U. In an example, the therapeutic effect is reduction of a symptom associated with a disorder selected from the group consisting of hemifacial spasm, adult onset spasmodic torticollis, anal fissure, blepharospasm, cerebral palsy, headaches, strabismus, temporomandibular joint disorder, neurologic pain, overactive bladder, rhinitis, sinusitis, acne, dystonia, dystonic contractions, hyperhidrosis, and hypersecretion of a gland controlled by the cholinergic nervous system. In certain examples, the duration of the treatment interval comprises greater than 3 months; greater than 4 months; greater than 5 months; greater than 6 months; greater than 7 months; greater than 8 months; greater than 9 months; or at least 6 months through 10 months.

Claims:

1. Use of botulinum toxin in the manufacture of a sterile injectable composition for achieving an extended duration cosmetic effect in an individual, wherein a treatment dose of the sterile injectable composition is to be administered by injection into an area of the individual in need of treatment to achieve the cosmetic effect following a treatment with the composition;

wherein the composition comprises a pharmaceutically acceptable diluent suitable for injection; and

a botulinum toxin of serotype A having a molecular weight of 150 kDa; and

a positively charged carrier has the amino acid sequence RKKRRQRRRG-$(K)_{15}$-GRKKRRQRRR;

wherein the botulinum toxin component is to be administered to the individual in a treatment dose of 40 U;

wherein the positively charged carrier is non-covalently associated with the botulinum toxin component; and

wherein the treatment dose of the composition administered by injection to the individual achieves the extended duration cosmetic effect having at least a 6 month duration of effect, wherein the cosmetic effect is a reduction in the appearance of glabellar lines.

2. A method of reducing wrinkles, lines, or furrows in a glabellar region of an individual in need thereof, the method comprising:

administering to the individual a composition comprising:

a pharmaceutically acceptable diluent for injection;

a botulinum toxin of serotype A having a molecular weight of 150 kDa; and

a positively charged carrier has the amino acid sequence RKKRRQRRRG-$(K)_{15}$-GRKKRRQRRR;

wherein the botulinum toxin is administered to the individual in an amount of 40 U;

wherein the positively charged carrier is non-covalently associated with the botulinum component; and

wherein the administration of the composition provides at least a six month duration of effect in reducing the wrinkles, lines, or furrows in the individual.

3. The method according to claim 2, wherein the wrinkles, lines, or furrows comprise glabellar lines.

4. The method or use according to any one of claims 1 to 3, wherein the composition does not locally diffuse from the site of injection following injection.

5. The method or use according to any one of claims 1 to 4, wherein the duration of treatment effect comprises greater than 7 months.

6. The method or use according to any one of claims 1 to 5, wherein the duration of treatment effect comprises greater than 8 months.

7. The method or use according to any one of claims 1 to 6, wherein the duration of treatment effect comprises 9 months.

8. A sterile injectable composition comprising:

a botulinum toxin of serotype A having a molecular weight of 150 kDa, in a dosage amount of 40 U; and

a positively charged carrier has the amino acid sequence RKKRRQRRRG-$(K)_{15}$-GRKKRRQRRR; and

a pharmaceutically acceptable diluent for injection;

wherein the positively charged carrier is non-covalently associated with the botulinum toxin component; and

wherein the composition provides a cosmetic effect of reducing the appearance of glabellar lines which endures for at least 20 to 24 weeks following a single treatment of an individual with the injectable composition.

9. A method of treating an individual in need of treatment with injectable botulinum toxin, wherein the method of treatment comprises a treatment course having multiple treatment intervals with prolonged duration of effect and duration time between each treatment interval, the treatment course comprising:

administering by injection an initial treatment dose of a sterile injectable composition into an area of the individual in need of treatment to achieve a cosmetic effect following the initial treatment with the composition;

wherein the composition comprises a pharmaceutically acceptable diluent suitable for injection;

a botulinum toxin of serotype A having a molecular weight of 150 kDa; and

a positively charged carrier has the amino acid sequence RKKRRQRRRG-$(K)_{15}$-GRKKRRQRRR; and

wherein the botulinum toxin component is administered to the individual in a treatment dose of 40 U;

wherein the positively charged carrier is non-covalently associated with the botulinum toxin component;

wherein the initial treatment dose of the composition administered by injection to the individual provides a cosmetic effect lasting through at least 6 months, wherein the cosmetic effect is reducing the appearance of glabellar lines; and

administering subsequent treatment doses of the composition by injection to the individual at treatment intervals comprising a duration of greater than or equal to 6 months to at least 9 months following the initial treatment dose and between each subsequent treatment dose.

10. The method according to claim 9, wherein the composition does not locally diffuse from the site of injection following injection.

11. The method according to any one of claims 9 to 10, wherein the duration of the treatment interval comprises greater than 6 months.

12. The method according to any one of claims 9 to 11, wherein the duration of the treatment interval comprises greater than 7 months.

13. The method according to any one of claims 9 to 12, wherein the duration of the treatment interval comprises greater than 8 months.

14. The method according to any one of claims 9 to 13, wherein the duration of the treatment interval comprises greater than 9 months.

15. The use, composition or method according to any one of the preceding claims, wherein the positively charged carrier is present in the composition in a ratio of 1-1000 ng/U of the botulinum toxin.

16. The use, composition or method according to any one of the preceding claims, wherein the composition comprises a non-reducing disaccharide, a non-ionic surfactant, and a physiologically compatible buffer to buffer in the range of 4.5 to 7.5.

17. The use, composition or method according to any one of the preceding claims, wherein the composition comprises a non-reducing disaccharide, polysorbate, and a histidine buffer.

18. The use, composition or method according to any one of the preceding claims, wherein the composition comprises a non-reducing disaccharide selected from sucrose or trehalose, polysorbate, and a histidine buffer.

19. The use, composition or method according to any one of claims 15 to 18, wherein the non-reducing disaccharide is trehalose.

20. The use, composition or method according to any one of claims 15 to 18, wherein the non-reducing disaccharide is sucrose.