CLAIMS

1. A polypeptide comprising a modified receptor binding domain of *Clostridial botulinum* serotype B (B-H_c) comprising a substitution mutation corresponding to a Y1183M substitution mutation in serotype B, strain 1, in which the substitution mutation produces enhanced binding of the modified B-H_c to human Syt II as compared to an identical molecule lacking the substitution mutation.

2. A botulinum neurotoxin (BoNT) polypeptide comprising:

(a) a protease domain;

(b) a protease cleavage site;

(c) a translocation domain; and

(d) a modified receptor binding domain of *Clostridial botulinum* serotype B (B-H_c), comprising a substitution mutation corresponding to a Y1183M substitution mutation in serotype B, strain 1 of SEQ ID NO: 4, in which the substitution mutation produces enhanced binding of the modified B-H_c to human Syt II as compared to an identical molecule lacking the substitution mutation.

3. A polypeptide or BoNT polypeptide according to Claim 1 or 2, in which the modified B-H_c is of strain 1.

4. A BoNT polypeptide according to Claim 2 or 3, in which the protease domain, translocation domain, and protease cleavage site are from a serotype selected from the group consisting of A, B, C, D, E, F, G, and combinations thereof, such as in which the protease domain, translocation domain, and protease cleavage site are from serotype B, strain 1 or serotype A, strain 1.

5. A polypeptide or BoNT polypeptide according to any preceding claim, in which the modified (B-H_c) comprises two substitution mutations.

6. A chimeric molecule comprising a first portion that is a modified receptor binding domain of *Clostridial botulinum* serotype B (B-H_c) linked to a second portion, in which the modified B-H_c comprises a Y to M substitution mutation at a position corresponding to Y1183 in serotype B, strain 1 of SEQ ID NO: 4, in which the substitution mutation produces

enhanced binding of the modified B-H_c to human Syt II as compared to an identical molecule lacking the substitution mutation.

7. A chimeric molecule according to Claim 6, in which the modified B-H_c comprises two substitution mutations.

8. A chimeric molecule according to Claim 6 or 7, in which the first portion and the second portion are linked covalently or are linked non-covalently; in which the second portion is selected from the group consisting of a small molecule, a nucleic acid, a short polypeptide and a protein; in which the second portion is a bioactive molecule; or in which the second portion is a therapeutic polypeptide or non-polypeptide drug.

9. A nucleic acid, such as a vector, comprising a nucleotide sequence that encodes a polypeptide, BoNT polypeptide or chimeric molecule according to any preceding claim.

10. A cell expressing a polypeptide, BoNT polypeptide or chimeric molecule according to any of Claims 1 to 8 or comprising a nucleic acid or vector according to Claim 9.

11. A pharmaceutical composition comprising a polypeptide, BoNT polypeptide or chimeric molecule according to any of Claims 1 to 8, a nucleic acid or vector according to Claim 9 or a cell according to Claim 10, and optionally comprising a pharmaceutically acceptable excipient.

12. A kit comprising a pharmaceutical composition according to Claim 11 and directions for therapeutic administration of the pharmaceutical composition.

13. A method of producing a polypeptide or botulinum neurotoxin (BoNT) polypeptide, the method comprising the steps of culturing a cell according to Claim 10 under conditions in which the polypeptide or BoNT polypeptide is produced, and optionally recovering the polypeptide or BoNT polypeptide from the culture.

14. A polypeptide, botulinum neurotoxin (BoNT) polypeptide, or chimeric molecule according to any of Claims 1 to 8, a nucleic acid according to Claim 9, a cell according to Claim 10, or a pharmaceutical composition according to Claim 11, for use in medicine.

15. A polypeptide, botulinum neurotoxin (BoNT) polypeptide, or chimeric molecule according to any of Claims 1 to 8, a nucleic acid according to Claim 9, a cell according to

Claim 10, or a pharmaceutical composition according to Claim 11, for use in treating a condition associated with unwanted neuronal activity.

16. A polypeptide, botulinum neurotoxin (BoNT) polypeptide, chimeric molecule, nucleic acid, cell or pharmaceutical composition according to Claim 14 or 15 for a use as specified therein, in which the use comprises administering a therapeutically effective amount of the polypeptide, BoNT polypeptide, chimeric molecule, nucleic acid, cell, or pharmaceutical composition to a subject to thereby contact one or more neurons exhibiting unwanted neuronal activity.

17. A polypeptide, botulinum neurotoxin (BoNT) polypeptide, chimeric molecule, nucleic acid, cell, or pharmaceutical composition according to Claim 14, 15 or 16 for a use as specified therein, in which the use comprises treating a condition selected from the group consisting of spasmodic dysphonia, spasmodic torticollis, laryngeal dystonia, oromandibular dysphonia, lingual dystonia, cervical dystonia, focal hand dystonia, blepharospasm, strabismus, hemifacial spasm, eyelid disorder, cerebral palsy, focal spasticity and other voice disorders, spasmodic colitis, neurogenic bladder, anismus, limb spasticity, tics, tremors, bruxism, anal fissure, achalasia, dysphagia and other muscle tone disorders and other disorders characterized by involuntary movements of muscle groups, lacrimation, hyperhydrosis, excessive salivation, excessive gastrointestinal secretions, secretory disorders, pain from muscle spasms, headache pain, and dermatological or aesthetic/cosmetic conditions.

18. Use of a polypeptide, botulinum neurotoxin (BoNT) polypeptide or chimeric molecule according to any of Claims 1 to 8, a nucleic acid according to Claim 9, or a cell according to Claim 10, in the preparation of a medicament for the treatment or prevention of a condition associated with unwanted neuronal activity, such as a condition selected from the group consisting of: spasmodic dysphonia, spasmodic torticollis, laryngeal dystonia, oromandibular dysphonia, lingual dystonia, cervical dystonia, focal hand dystonia, blepharospasm, strabismus, hemifacial spasm, eyelid disorder, cerebral palsy, focal spasticity and other voice disorders, spasmodic colitis, neurogenic bladder, anismus, limb spasticity, tics, tremors, bruxism, anal fissure, achalasia, dysphagia and other muscle tone disorders and other disorders characterized by involuntary movements of muscle groups, lacrimation, hyperhydrosis, excessive salivation, excessive gastrointestinal secretions, secretory disorders, pain from muscle spasms, headache pain, and dermatological or aesthetic/cosmetic conditions.