CLAIMS

1. A polypeptide comprising a modified receptor binding domain of *Clostridial botulinum* serotype B (B-H_c) comprising one or more substitution mutations corresponding to substitution mutations in serotype B, strain 1, selected from the group consisting of E1191M; E1191I; E1191Q; E1191T; S1199F; S1199L; S1201V; V1118M; and combinations thereof, in which the substitution mutation produces enhanced binding of the modified B-Hc to human SytII 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 one or more substitution mutations corresponding to substitution mutations in serotype B, strain 1, selected from the group consisting of: E1191M; E1191I; E1191Q; E1191T; S1199F; S1199L; S1201V; V1118M; and combinations thereof, in which the substitution mutation produces enhanced binding of the modified B-Hc to human SytII as compared to an identical molecule lacking the substitution mutation.

3. 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-Hc), comprising a substitution mutation at a position corresponding to S1199 or S1201 of serotype B, 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 serotype selected from the group consisting of A, B, C, D, E, F, G, and combinations thereof, preferably in which the protease

domain, translocation domain, and protease cleavage site are from serotype B, strain 1 or from serotype A, strain 1.

5. A polypeptide or BoNT polypeptide according to any preceding claim, in which the modified (B-Hc) comprises two substitution mutations, preferably in which the two substitution mutations correspond to E1191M and S1199Y, E1191M and S1199L, E1191M and S1199F, E1191Q and S1199L, E1191Q and S1199Y, or E1191Q and S1199F.

6. A polypeptide or BoNT polypeptide according to any preceding claim that is a chimeric molecule comprising a first portion that is the modified receptor binding domain of *Clostridial botulinum* serotype B (B-H_c) linked to a second portion.

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

8. A nucleic acid, preferably a vector, comprising a nucleotide sequence that encodes a polypeptide or BoNT polypeptide according to any preceding claim.

9. A cell comprising a nucleic acid according to Claim 8 or expressing a polypeptide or BoNT polypeptide according to any of Claims 1 to 7.

10. A pharmaceutical composition comprising a polypeptide or botulinum neurotoxin (BoNT) polypeptide according to any of Claims 1 to 7, a nucleic acid according to Claim 8.

11. A pharmaceutical composition according to Claim 10, further comprising a pharmaceutically acceptable excipient.

12. A kit comprising a pharmaceutical composition according to Claim 10 or 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 host cell according to Claim 9 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 or botulinum neurotoxin (BoNT) polypeptide according to any of Claims 1 to 7, or a pharmaceutical composition according to Claim 10 or 11, for use in therapy.

15. A polypeptide or botulinum neurotoxin (BoNT) polypeptide according to any of Claims 1 to 7, or a pharmaceutical composition according to Claim 10 or 11, for use in treating a condition associated with unwanted neuronal activity, preferably in which the condition is 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.