

CLAIMS

1. A fusion protein comprising:
a CDKL5 polypeptide sequence, wherein the CDKL5 polypeptide sequence comprises SEQ ID NO:2 or SEQ ID NO: 16; and
a TATk polypeptide sequence, wherein the TATk polypeptide sequence has about 90% to about 100% sequence identity to SEQ ID NO: 4, wherein the TATk polypeptide is operatively coupled to the CDKL5 polypeptide.
2. The fusion protein of claim 1, further comprising an Igk-chain leader sequence polypeptide, wherein the Igk-chain leader sequence is operatively coupled to the CDKL5 polypeptide.
3. The fusion protein of claim 1, further comprising a reporter protein polypeptide, wherein the reporter protein polypeptide is operatively coupled to the CDKL5 polypeptide.
4. The fusion protein of claim 1, further comprising a protein tag polypeptide, wherein the protein tag polypeptide is operatively coupled to the CDKL5 polypeptide.
5. The fusion protein of claim1, wherein the fusion protein has a polypeptide sequence according to SEQ ID NO: 8, SEQ ID NO: 10, SEQ ID NO: 12, or SEQ ID NO: 14.
6. The fusion protein of claim 1, wherein the fusion protein increases neurite growth, elongation, branch number, or branch density in a brain of a treated subject as compared to an untreated control subject.
7. The fusion protein of claim 1, wherein the fusion protein reduces neuron apoptosis in the brain of a treated subject as compared to an untreated control subject.

8. A pharmaceutical formulation comprising:
 - a therapeutically effective amount of a fusion protein comprising:
 - a CDKL5 polypeptide sequence, wherein the CDKL5 polypeptide sequence comprises SEQ ID NO:2 or SEQ ID NO: 16; and
 - a TATk polypeptide sequence, wherein the TATk polypeptide sequence has about 90% to about 100% sequence identity to SEQ ID NO: 4, wherein the TATk polypeptide is operatively coupled to the CDKL5 polypeptide; and
 - a pharmaceutically acceptable carrier.
9. The pharmaceutical formulation of claim 8, wherein the fusion protein further comprises an Igk-chain leader sequence polypeptide, wherein the Igk-chain leader sequence is operatively coupled to the CDKL5 polypeptide.
10. The pharmaceutical formulation of claim 8, wherein the fusion protein further comprises a reporter protein polypeptide, wherein the reporter protein polypeptide is operatively coupled to the CDKL5 polypeptide.
11. The pharmaceutical formulation of claim 8, wherein the fusion protein further comprises a protein tag polypeptide, wherein the protein tag polypeptide is operatively coupled to the CDKL5 polypeptide.
12. The pharmaceutical formulation of claim 8, wherein the fusion protein has a polypeptide sequence according to SEQ ID NO: 8, SEQ ID NO: 10, SEQ ID NO: 12, or SEQ ID NO: 14.
13. The pharmaceutical formulation of claim 8, wherein the therapeutically effective amount of the fusion protein treats one or more symptoms of a CDKL5 deficiency, Rett syndrome, or Rett syndrome variant in a treated subject as compared to an untreated control subject.
14. The pharmaceutical formulation of claim 8, wherein the therapeutically effective amount of the fusion protein increases neurite growth, elongation, branch number, or branch density in a brain of a treated subject as compared to an untreated control subject.

15. The pharmaceutical formulation of claim 8, wherein the therapeutically effective amount of the fusion protein reduces neuron apoptosis in the brain of a treated subject as compared to an untreated control subject.
16. The pharmaceutical formulation of claim 8, wherein the therapeutically effective amount of the fusion protein improves motor function in a treated subject as compared to an untreated control subject.
17. The pharmaceutical formulation of claim 8, wherein the therapeutically effective amount of the fusion protein improves cognitive function in a treated subject as compared to an untreated control subject.
18. The fusion protein according to claim 1 for use in the treatment of a CDKL5 deficiency, Rett syndrome, or a Rett syndrome variant.
19. Use of the fusion protein according to claim 1 in the manufacture of a medicament for the treatment of a subject in need thereof or is suspected of having a CDKL5 deficiency, Rett syndrome, or a Rett syndrome variant.
20. The use according to claim 19, wherein the use is to treat one or more symptoms of a CDKL5 deficiency, Rett syndrome, or a Rett syndrome variant in a treated subject as compared to an untreated control subject.
21. The pharmaceutical formulation according to claim 8 for use in the treatment of a CDKL5 deficiency, Rett syndrome, or a Rett syndrome variant.
22. Use of the pharmaceutical formulation according to claim 8 in the manufacture of a medicament for the treatment of a subject in need thereof or is suspected of having a CDKL5 deficiency, Rett syndrome, or a Rett syndrome variant.

23. The use according to claim 22, wherein the use is to treat one or more symptoms of a CDKL5 deficiency, Rett syndrome, or a Rett syndrome variant in a treated subject as compared to an untreated control subject.