

SUMMARY

[0004a] In one aspect, the present disclosure refers to a use of a pharmaceutically effective amount of a composition comprising a peptide having the sequence Thr Pro His Thr His Gln Xaa Thr Pro Glu (SEQ ID NO:4) in the manufacture of a medicament for treating a retinal angiogenic disease in a subject, wherein the composition is to be administered to the subject orally, by intravenous injection, or by intravitreal injection.

[0004b] In another aspect, the present disclosure refers to a use of a composition comprising a peptide having the sequence SEQ ID NO:1 in the manufacture of a medicament for treating a retinal angiogenic disease in a subject, wherein the composition is to be administered to a subject with retinal angiogenic disease not responsive to anti-VEGF therapy.

[0004c] In another aspect, the present disclosure refers to a use of a pharmaceutically effective amount of a composition comprising a peptide N having the sequence Thr Pro His Thr His Asn Xaa Thr Pro Glu wherein Xaa is homoarginine (SEQ ID NO:3) in the manufacture of a medicament for treating a retinal angiogenic disease, wherein the composition is to be administered to the subject orally, by intravenous injection, or by intravitreal injection.

[0004d] In another aspect, the present disclosure refers to a use of a pharmaceutically effective amount of a composition comprising a peptide Q having the sequence Thr Pro His Thr His Asn Arg Thr Pro Glu (SEQ ID NO:1) in the manufacture of a medicament for treating a retinal angiogenic disease, wherein the composition is to be administered to the subject orally, by intravenous injection, or by intravitreal injection.

[0004e] In another aspect, the present disclosure refers to a method of manufacturing a composition as disclosed herein, wherein the peptides are synthesized by solid phase Fmoc chemistry.

[0005] Provided herein is a method of treating a retinal angiogenic disease in a subject. The methods include administering to the subject a pharmaceutically effective amount of a composition comprising a peptide having the sequence Thr Pro His Thr His Asn Arg Thr Pro Glu (SEQ ID NO:1). The composition can be administered to the subject orally, by intravenous injection, or by intravitreal injection, or by sublingual delivery wherein administration treats the retinal angiogenic disease in the subject.

[0006] Optionally, the composition comprises 2 to 50 mg/kg body weight (Bwt) of the peptide and is administered by intravenous injection. Optionally, the composition comprises 0.1 µg/kg to 5 mg/kg Bwt of the peptide and is administered by intravitreal injection. Optionally, the composition comprises 2 to 10 mg/kg Bwt of the peptide and is administered orally.

[0007] Optionally, the composition is administered via either intravenous (IV) or intravitreal (IVT) route at least once every 4 to 24 weeks. Optionally, the composition is administered orally at least once daily for 1 to 2 weeks at intervals of 6 months. In this treatment protocol, the composition is not administered during the 6 month interval. Optionally, for the subject not responsive to anti-VEGF therapy, for example, a VEGF antibody.

[0008] Optionally, the subject has age-related macular degeneration, retinopathy, or vascular occlusion. Optionally, the subject has diabetic retinopathy, diabetic macular edema, central retinal vein occlusion, branch retinal vein occlusion, or corneal neovascularization. Optionally, the subject is a human.

[0009] Also provided herein is a method of treating a retinal angiogenic disease in a subject. The methods include selecting a subject with retinal angiogenic disease not responsive to an anti-angiogenesis therapy, and administering to the subject a composition comprising a peptide having the sequence SEQ ID NO:1, wherein administration treats the retinal angiogenic disease in the subject. Optionally, the subject is not responsive to an anti-VEGF therapy.

[0010] Optionally, the composition disclosed herein is formulated for intravenous administration, for intravitreal injection, or for oral administration. Optionally, the subject has age-related macular degeneration, retinopathy, or vascular occlusion. Optionally, the

WHAT IS CLAIMED IS:

1. Use of a pharmaceutically effective amount of a composition comprising a peptide having the sequence Thr Pro His Thr His Gln Xaa Thr Pro Glu (SEQ ID NO:4) in the manufacture of a medicament for treating a retinal angiogenic disease in a subject, wherein the composition is to be administered to the subject orally, by intravenous injection, or by intravitreal injection.
2. The use of claim 1, wherein the composition comprises 2 to 50 mg/kg Bwt of the peptide and is to be administered by intravenous injection.
3. The use of claim 1, wherein the composition comprises 0.1 µg/kg to 2 mg/kg Bwt of the peptide and is to be administered by intravitreal injection.
4. The use of claim 1, wherein the composition comprises 2 to 10 mg/kg Bwt of the peptide and is to be administered orally.
5. The use of claim 1, wherein the composition is to be administered via either intravenous (IV) or intravitreal (IVT) route at least once every 4 to 10 weeks.
6. The use of claim 1, wherein the composition is to be administered orally at least once daily for 1 to 2 weeks at intervals of 6 months.
7. The use of claim 1, wherein subject is not responsive to anti-VEGF therapy.
8. The use of claim 2, wherein the anti-VEGF therapy is an anti-VEGF antibody.
9. The use of any one of claims 1-8, wherein the subject has age-related macular degeneration, retinopathy, or vascular occlusion.
10. The use of any one of claims 1-8, wherein the subject has diabetic retinopathy, diabetic macular edema, central retinal vein occlusion, branch retinal vein occlusion, or corneal neovascularization.

11. The use of any one of claims 1-10, wherein the subject is a human.
12. Use of a composition comprising a peptide having the sequence SEQ ID NO:1 in the manufacture of a medicament for treating a retinal angiogenic disease in a subject, wherein the composition is to be administered to a subject with retinal angiogenic disease not responsive to anti-VEGF therapy.
13. The use of claim 12, wherein the composition is formulated for intravenous administration.
14. The use of claim 12, wherein the composition is formulated for intravitreal injection.
15. The use of claim 12, wherein the composition is formulated for oral administration.
16. The use of any one of claims 12-15, wherein the subject has age-related macular degeneration, retinopathy, or vascular occlusion.
17. The use of any one of claims 12-15, wherein the subject has diabetic retinopathy, diabetic macular edema, central retinal vein occlusion, branch retinal vein occlusion, or corneal neovascularization.
18. The use of any one of claims 12-17, wherein the subject is not responsive to anti-angiogenesis therapy.
19. The use of claim 18, wherein the anti-angiogenesis therapy is an anti-VEGF therapy.
20. The use of any one of claim 19, wherein the anti-VEGF therapy is an anti-VEGF antibody.
21. The use of any one of claims 12-20, wherein the subject is a human.

22. Use of a pharmaceutically effective amount of a composition comprising a peptide N having the sequence Thr Pro His Thr His Asn Xaa Thr Pro Glu wherein Xaa is homoarginine (SEQ ID NO:3) in the manufacture of a medicament for treating a retinal angiogenic disease, wherein the composition is to be administered to the subject orally, by intravenous injection, or by intravitreal injection.

23. Use of a pharmaceutically effective amount of a composition comprising a peptide Q having the sequence Thr Pro His Thr His Asn Arg Thr Pro Glu (SEQ ID NO:1) in the manufacture of a medicament for treating a retinal angiogenic disease, wherein the composition is to be administered to the subject orally, by intravenous injection, or by intravitreal injection.

24. A method of manufacturing a composition of any of the above claims, wherein the peptides are synthesized by solid phase Fmoc chemistry.