CLAIMS

1. An adeno-associated virus (AAV) particle, comprising:

(i) a nucleic acid construct comprising a coding sequence operably linked to a promoter, wherein the coding sequence encodes a vascular endothelial growth factor (VEGF) binding agent or a portion thereof; and

(ii) an AAV Anc80 capsid.

2. The AAV particle of claim 1, wherein the promoter is a CAG promoter, a CBA promoter, a CMV promoter, or a CB7 promoter.

3. The AAV particle of claim 1 or 2, wherein the VEGF binding agent is or comprises an antibody or a fragment thereof.

4. The AAV particle of claim 3, wherein the antibody fragment comprises a Fab fragment, a Fab' fragment, a F(ab')2 fragment, a Fd fragment, a Fd' fragment, a complementarity determining region (CDR), a single chain Fv, an Fc domain, or any combination thereof.

5. The AAV particle of any one of claims 1-4, wherein the VEGF binding agent is or comprises an immunoglobulin heavy chain, an immunoglobulin light chain, or any combination thereof.

6. The AAV particle of any one of claims 1-5, wherein the VEGF binding agent comprises:

(i) a polypeptide comprising the amino sequence of SEQ ID NO: 16,

(ii) a polypeptide comprising the amino sequence of SEQ ID NO: 20, or

(iii) any combination thereof.

7. The AAV particle of claim 6, wherein the VEGF binding agent is or comprises ranibizumab.

8. The AAV particle of any one of claims 1-7, wherein the coding sequence comprises:

(i) a nucleic acid sequence comprising SEQ ID NO: 13,
(ii) a nucleic acid sequence comprising SEQ ID NO: 19, or
(iii) any combination thereof.

9. The AAV particle of any one of claims 1-8, wherein the coding sequence comprises one or more nucleic acid sequences that each encode a signal peptide.

10. The AAV particle of claim 9, wherein at least one nucleic acid sequence encodes an interleukin 2 (IL2) signal peptide.

11. The AAV particle of any one of claims 1-10, wherein the coding sequence comprises one or more sequences encoding a self-cleaving peptide.

12. The AAV particle of claim 11, wherein the self-cleaving peptide is a thosea asigna virus 2A (T2A) peptide.

13. The AAV particle of any one of claims 1-12, wherein the coding sequence is or comprises a nucleic acid sequence encoding the amino acid sequence of SEQ ID NO: 21.

14. The AAV particle of any one of claims 1-13, further comprising two AAV inverted terminal repeats (ITRs), wherein the two AAV ITRs flank the coding sequence and promoter.

15. The AAV particle of claim 14, wherein the two AAV ITRs are or are derived from AAV2 ITRs.

16. The AAV particle of claim 14 or 15, wherein the two AAV ITRs comprise a 5` ITR comprising a nucleic acid sequence according to SEQ ID NO: 45 or 47, and a 3` ITR comprising a nucleic acid sequence according to SEQ ID NO: 46 or 48.

17. The AAV particle of any one of the preceding claims, wherein the construct comprises a nucleic acid sequence according to any of SEQ ID NOs: 90, 91, or 92.

18. The AAV particle of claim any one of the preceding claims, wherein the AAV Anc80 capsid is an AAV Anc80L65 capsid.

19. The AAV particle of any one of the preceding claims, wherein the AAV Anc80 capsid comprises a polypeptide according to SEQ ID NO: 113 or SEQ ID NO: 114.

20. A composition comprising the AAV particle of any one of claims 1-19.

21. The composition of claim 20, wherein the composition is a pharmaceutical composition comprising a pharmaceutically acceptable carrier and/or excipients.

22. The composition of claim 20 or 21, wherein the composition is formulated at a dose of about 1 x 10^{11} vg/mL to about 1 x 10^{15} vg/mL.

23. The composition of claim 22, wherein the composition is formulated at a dose of about 2.5 x 10^{12} vg/mL.

24. The composition of claim 22, wherein the composition is formulated at a dose of about 5 x 10^{12} vg/mL.

25. The composition of claim 22, wherein the composition is formulated at a dose of about 1 x 10^{13} vg/mL.

26. The composition of any one of claims 20-22, wherein the composition is formulated at a dose of about 1 x 10^{10} vg/cochlea to about 1 x 10^{13} vg/cochlea.

27. The composition of claim 26, wherein the composition is formulated at a dose of about 2.3 x 10^{11} vg/cochlea.

28. The composition of claim 26, wherein the composition is formulated at a dose of about 4.5 x 10^{11} vg/cochlea.

29. The composition of claim 26, wherein the composition is formulated at a dose of about 9 x 10^{11} vg/cochlea.

30. The composition of any one of claims 20-29, formulated for delivery to the inner ear.

31. The composition of any one of claims 20-30, formulated for intracochlear administration.

32. The composition of any one of claims 20-31, wherein the composition comprises a synthetic perilymph solution.

33. The composition of claim 32, wherein the synthetic perilymph solution comprises: about 20-200mM NaCl, about 1-5 mM KCl, about 0.1-10mM $CaCl_2$, about 1-10mM glucose, about 2-50 mM HEPES, a pH of about 6-9, or any combination thereof.

34. The composition of any one of claims 20-32, wherein the composition comprises: Sodium Phosphate Dibasic, Monopotassium Phosphate, Potassium Chloride, Sodium Chloride, Poloxamer 188, or any combination thereof.

35. The composition of claim 34, wherein the composition comprises:
(i) about 1-20mM Sodium Phosphate Dibasic;
(ii) about 0.1-5mM Monopotassium Phosphate;
(iii) about 0.1-10mM Potassium Chloride;
(iv) about 100-1000mM Sodium Chloride;
(v) about 0.0001-0.001% Poloxamer 188; or
(vi) any combination of (i)-(v).

36. The composition of any one of claims 20-31, wherein the composition is administered at a volume of about 0.01mL to about 0.1 mL.

37. Use of an AAV particle of any one of claims 1-19, for the manufacture of a medicament.

38. Use of a composition of any one of claims 20-36, for the manufacture of a medicament.

39. The use of claim 37 or 38, wherein the medicament is to be contacted with an inner ear cell.

40. The use of claim 39, comprising the medicament to be introduced into an inner ear of a subject.

41. The use of claim 40, further comprising a hearing level of the subject to be measured.

42. The use of claim 41, further comprising comparing the hearing level of the subject to a reference hearing level.

43. The use of claim 42, wherein the hearing level of the subject is measured after the AAV particle of any one of claims 1-19, or the composition of any one of claims 20-36 has been introduced, and the reference hearing level is a hearing level of the subject that was measured before the AAV particle of any one of claims 1-19, or the composition of any one of claims 20-36 had been introduced.

44. The use of any one of claims 40-43, further comprising a level of a VEGF binding agent or a portion thereof to be measured in a subject.

45. The use of claim 44, further comprising comparing the level of the VEGF binding agent or a portion thereof in the subject to a reference level of VEGF binding agent or a portion thereof.

46. The use of any one of claims 40-45, further comprising measuring a volume of a tumor in a subject.

47. The use of claim 46, further comprising comparing a volume of a tumor in the subject to a reference tumor volume.

48. Use of an AAV particle of any one of claims 1-19, or a composition of any one of claims 20-36, in the manufacture of a medicament for treating of an otological disease characterized by neovascularization and/or one or more symptoms associated with the otological disease.

49. Use of an AAV particle of any one of claims 1-19, or a composition of any one of claims 20-36, in the manufacture of a medicament for treating an inner ear disorder.

50. The use of claim 49, wherein the inner ear disorder is vestibular schwannoma, or neurofibromatosis type II.

51. The use of any one of claims 48-50, wherein the mammal is a human.

52. A kit comprising an AAV particle of any one of claims 1-19, or a composition of any one of claims 20-36.

53. A construct comprising a coding sequence operably linked to a promoter, wherein the coding sequence encodes a vascular endothelial growth factor (VEGF) binding agent or a portion thereof.

54. A method comprising, contacting a cell with:

(i) a construct comprising a coding sequence operably linked to a promoter, wherein the coding sequence encodes a vascular endothelial growth factor (VEGF) binding agent or a portion thereof; and

(ii) one or more constructs comprising an AAV Rep gene, AAV Cap gene, AAV VA gene, AAV E2a gene, and AAV E4 gene.