

WE CLAIM:

1. A polypeptide comprising three active domains wherein one domain is an anti-CD4 Adnectin protein, a second domain is a gp41 binding moiety and a third domain is a HIV fusion peptide inhibitor moiety.

2. A polypeptide comprising three active domains wherein one domain is a CD4 binding moiety, a second domain is an anti-N17 Adnectin protein and a third domain is a HIV fusion peptide inhibitor moiety.

3. The polypeptide of claim 1 or 2 wherein the three domains are connected to each other in any order by linkers.

4. The polypeptide of claim 1 or 2 further comprising one or more pharmacokinetic (PK) moieties selected from the group consisting of polyethylene glycol, sialic acid, Fc, Fc fragment, transferrin, serum albumin, a serum albumin binding protein, and a serum immunoglobulin binding protein.

5. The polypeptide of claim 4, wherein the PK moiety is Fc.

6. The polypeptide of claim 5, wherein the Fc is attached to the N-terminus of the polypeptide.

7. The polypeptide of claim 4, wherein the PK moiety is human serum albumin.

8. The polypeptide of claim 7, wherein the human serum albumin is attached to the N-terminus of the polypeptide.

9. The polypeptide of claim 1 wherein the anti-CD4 Adnectin protein comprises an amino acid sequence at least 80%, 85%, 90%, 95%, 98%, 99% or 100% identical to the amino acid sequence of SEQ ID NOs: 95-114.

10. The polypeptide of claim 2 wherein the anti-N17 Adnectin protein comprises an amino acid sequence at least 80%, 85%, 90%, 95%, 98%, 99% or 100% identical to the amino acid sequence of SEQ ID NO: 115-371.

5 11. The polypeptide of claim 1 or 2 wherein the HIV fusion peptide inhibitor comprises an amino acid sequence at least 80%, 85%, 90%, 95%, 98%, 99% or 100% identical to the amino acid sequence of SEQ ID NO: 372-392.

10 12. A polypeptide comprising two active domains wherein one domain is an anti-CD4 Adnectin protein and the other domain is a gp41 binding moiety or a HIV fusion peptide inhibitor moiety.

15 13. A polypeptide comprising two active domains wherein one domain is an anti-N17 Adnectin protein and the other domain is a CD4 binding moiety or a HIV fusion peptide inhibitor moiety.

14. The polypeptide of claim 12 or 13 wherein the two domains are connected to each other in any order by linkers.

20 15. The polypeptide of claim 12 or 13 further comprising one or more pharmacokinetic (PK) moieties selected from the group consisting of polyethylene glycol, sialic acid, Fc, Fc fragment, transferrin, serum albumin, a serum albumin binding protein, and a serum immunoglobulin binding protein.

25 16. The polypeptide of claim 15, wherein the PK moiety is Fc.

17. The polypeptide of claim 16, wherein the Fc is attached to the N-terminus of the polypeptide.

30 18. The polypeptide of claim 15, wherein the PK moiety is human serum albumin.

19. The polypeptide of claim 18, wherein the human serum albumin is attached to the N-terminus of the polypeptide.

20. A polypeptide comprising three active domains wherein one domain is an anti-CD4 Adnectin protein, a second domain is an anti-N17 Adnectin protein and the third domain is a HIV fusion peptide inhibitor.

21. The polypeptide of claim 20 wherein the three domains are connected to each other in any order by linkers.

22. The polypeptide of claims 20 or 21 further comprising one or more pharmacokinetic (PK) moieties selected from the group consisting of polyethylene glycol, sialic acid, Fc, Fc fragment, transferrin, serum albumin, a serum albumin binding protein, and a serum immunoglobulin binding protein.

23. The polypeptide of claim 22, wherein the PK moiety is Fc.

24. The polypeptide of claim 23, wherein the Fc is attached to the N-terminus of the polypeptide.

25. The polypeptide of claim 22, wherein the PK moiety is human serum albumin.

26. The polypeptide of claim 25, wherein the human serum albumin is attached to the N-terminus of the polypeptide.

27. A polypeptide comprising an amino acid sequence at least 80%, 85%, 90%, 95%, 98%, 99% or 100% identical to the non-linker regions of SEQ ID NO: 3, 5, 7 or 9.

28. The polypeptide of claim 27 further comprising one or more pharmacokinetic (PK) moieties selected from the group consisting of polyethylene glycol,

sialic acid, Fc, Fc fragment, transferrin, human serum albumin, a serum albumin binding protein, and a serum immunoglobulin binding protein.

29. The polypeptide of claim 28, wherein the PK moiety is Fc.

30. The polypeptide of claim 29, wherein the Fc is attached to the N-terminus of the polypeptide.

31. The polypeptide of claim 28, wherein the PK moiety is human serum albumin.

32. The polypeptide of claim 31, wherein the human serum albumin is attached to the N-terminus of the polypeptide.

33. A polypeptide comprising an amino acid sequence at least 80%, 85%, 90%, 95%, 98%, 99% or 100% identical to the non-linker regions of SEQ ID NO: 4, 6, 8 or 10.

34. A polypeptide comprising the amino acid sequence shown in SEQ ID NO: 3.

35. A polypeptide comprising the amino acid sequence shown in SEQ ID NO: 4.

36. A polypeptide comprising the amino acid sequence shown in SEQ ID NO: 5.

37. A polypeptide comprising the amino acid sequence shown in SEQ ID NO: 6.

38. A polypeptide comprising the amino acid sequence shown in SEQ ID NO: 7.

39. A polypeptide comprising the amino acid sequence shown in SEQ ID NO:
8.

40. A polypeptide comprising the amino acid sequence shown in SEQ ID NO:
5 9.

41. A polypeptide comprising the amino acid sequence shown in SEQ ID NO:
10.

10 42. A polypeptide comprising two active domains wherein one domain is an
anti-N17 Adnectin protein and the second domain is a HIV fusion inhibitor peptide.

43. The polypeptide of claim 42 wherein the two domains are connected to each
other in any order by linkers.

15 44. The polypeptide of claims 42 or 43 further comprising one or more
pharmacokinetic (PK) moieties selected from the group consisting of polyethylene glycol,
sialic acid, Fc, Fc fragment, transferrin, serum albumin, a serum albumin binding protein,
and a serum immunoglobulin binding protein.

20 45. The polypeptide of claim 44, wherein the PK moiety is Fc.

46. The polypeptide of claim 45, wherein the Fc is attached to the N-terminus
of the polypeptide.

25 47. The polypeptide of claim 44, wherein the PK moiety is human serum
albumin.

30 48. The polypeptide of claim 47, wherein the human serum albumin is
attached to the N-terminus of the polypeptide.

49. A pharmaceutical composition comprising a polypeptide of any one of the preceding claims, and a carrier.

5 50. Use of an effective amount of the polypeptide or composition thereof according to any one of claims 1- 49 in the manufacture of a medicament for treating HIV in a subject.

10 51. A polypeptide or composition thereof according to any one of claims 1-49 for use in treating HIV in a subject.

52. An anti-CD4 Adnectin protein, wherein the Adnectin comprises an amino acid sequence that is at least 90% identical to the amino acid sequence of any one of SEQ ID NOs: 95-114.

15 53. An anti-N17 Adnectin protein, wherein the Adnectin comprises an amino acid sequence that is at least 90% identical to the amino acid sequence of any one of SEQ ID NOs: 115-371.