

## CLAIMS

1. A pharmaceutical composition comprising polyclonal immunoglobulin from an equine that has been hyper-immunized with a filovirus glycoprotein.
2. The composition of claim 1, wherein the immunoglobulin is purified from serum or plasma of the equine that has been hyper-immunized with the filovirus glycoprotein.
3. The composition of claim 2, wherein the purified immunoglobulin is IgG, or a fragment thereof.
4. The composition of claim 3, wherein at least 1%, 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 11%, 12%, 13%, 14%, 15%, 20%, or more of the purified IgG binds to the filovirus glycoprotein.
5. The composition of any one of claims 2 to 4, wherein the purified immunoglobulin can prevent or minimize symptoms in a subject infected with a filovirus.
6. The composition of any one of claims 1 to 5, wherein the filovirus is Ebola virus (EBOV), Sudan virus (SUDV), Bundibugyo virus (BDBV), Tai Forrest virus (TAFV), Reston virus (RESTV), or Marburg virus (MARV).
7. The composition of any one of claims 1 to 6, wherein the equine is immunized with a mucin-like domain-deleted filovirus spike glycoprotein.
8. The composition of any one of claims 1 to 7, wherein the transmembrane domain of the spike glycoprotein is deleted.
9. The composition of claim 7 or claim 8, wherein the spike glycoprotein comprises the GP1 subunit or a fragment thereof from MARV, EBOV, SUDV, BDBV, TAFV, RESTV, or a combination of GP1 subunits thereof.

10. The composition of claim 7 or claim 8, wherein the spike glycoprotein comprises the GP1 subunit or a fragment thereof and the GP2 subunit or a fragment thereof from MARV, EBOV, SUDV, BDBV, TAFV, RESTV, or a combination of GP1 and GP2 subunits thereof.
11. The composition of any one of claims 7 to 10, wherein the spike glycoprotein comprises an amino acid sequence that is at least 90%, at least 95%, or 100% identical to SEQ ID NOS: 2, 4, 6, 8, 10, or 12.
12. The composition of any one of claims 7 to 11, wherein the equine is immunized with the spike glycoprotein on days 0, 21, 42, and 63, respectively.
13. The composition of claim 12, wherein the polyclonal immunoglobulin is recovered as plasma on day 90 via plasmapheresis.
14. The composition of claim 12 or claim 13, wherein the spike glycoprotein comprises MARV GP-ΔTM, and wherein the recovered plasma has an EC50 titer for binding to MARV GP-ΔTM of at least  $10^2$ , at least  $5 \times 10^2$ , at least  $10^3$ , at least  $5 \times 10^3$ , at least  $10^4$ , at least  $5 \times 10^4$ , at least  $10^5$ , or at least  $5 \times 10^5$ , as determined by ELISA.
15. The composition of claim 13 or claim 14, wherein the spike glycoprotein comprises MARV GP-ΔTM, and wherein the purified IgG binds to MARV GP-ΔTM with an EC50 of less than 3  $\mu\text{g/ml}$ , less than 2.5  $\mu\text{g/ml}$ , less than 2  $\mu\text{g/ml}$ , less than 1.5  $\mu\text{g/ml}$ , or less than 1  $\mu\text{g/ml}$ , or less than 0.5  $\mu\text{g/ml}$ , as measured ELISA.
16. The composition of any one of claims 12 to 15, wherein two doses of about 100 mg/kg of the immunoglobulin administered to a mouse following a lethal challenge with a filovirus can protect the mouse against the lethal challenge.
17. The composition of any one of claims 7 to 11, wherein the equine is immunized with a prime-boost regimen.

18. The composition of claim 17, wherein the prime-boost regimen comprises priming with a filovirus virus-like particle (VLP) and boosting with the spike glycoprotein.
19. The composition of claim 18, wherein the VLP comprises a filovirus glycoprotein and a filovirus VP40.
20. The composition of claim 19, wherein the VLP further comprises the filovirus nucleoprotein (NP).
21. The composition of claim 18, wherein the prime dose is administered on day zero and day 21, respectively, and the boost dose is administered on day 42 and day 63, respectively.
22. The composition of claim 21, wherein the polyclonal immunoglobulin is recovered as plasma on day 90 via plasmapheresis.
23. The composition of any one of claims 17 to 22, wherein the prime dose comprises an EBOV VLP comprising GP, VP40, or NP, the boost dose comprises EBOV GP-ΔMuc, and wherein the recovered plasma has an EC50 titer for binding to EBOV GP-ΔTM of at least  $10^3$ , at least  $10^4$ , at least  $10^5$ , or at least  $5 \times 10^5$ , as determined by ELISA.
24. The composition of any one of claims 17 to 23, wherein the prime dose comprises an EBOV VLP comprising GP, VP40, or NP, the boost dose comprises EBOV GP-ΔMuc, and wherein the purified IgG binds to EBOV GP-ΔTM or EBOV GP-ΔMuc with an EC50 of less than 1 μg/ml, less than 0.9 μg/ml, less than 0.8 μg/ml, less than 0.7 μg/ml, less than 0.6 μg/ml, less than 0.5 μg/ml, less than 0.4 μg/ml, less than 0.3 μg/ml, less than 0.2 μg/ml, less than 0.1 μg/ml, or less than 0.09 μg/ml, as measured ELISA.
25. The composition of any one of claims 17 to 24, wherein two doses of about 100 mg/kg of the immunoglobulin administered to a mouse following a lethal challenge with a filovirus can protect the mouse against the lethal challenge.

26. A method for preparing the composition of any one of claims 1 to 25, comprising administering an amount of a filovirus immunogen to an equine sufficient to hyperimmunize the equine against protective antigens of the filovirus, wherein the immunogen comprises a filovirus spike glycoprotein; and recovering immunoglobulin from the equine.
27. The method of claim 26, wherein the immunoglobulin is recovered as plasma.
28. The method of claim 26 or claim 27, further comprising purifying the immunoglobulin recovered from the equine.
29. The method of claim 28, wherein the purified immunoglobulin comprises IgG or a fragment thereof.
30. A polyclonal immunoglobulin from an equine that has been hyper-immunized with a filovirus glycoprotein for use in preventing, treating, or managing a filovirus-mediated disease in a subject.
31. Use of a polyclonal immunoglobulin from an equine that has been hyper-immunized with a filovirus glycoprotein in the manufacture of a medicament for the treatment, prevention or management of a filovirus-mediated disease.
32. The use of claim 31, wherein the immunoglobulin is purified from serum or plasma of the equine that has been hyper-immunized with the filovirus glycoprotein.
33. The use of claim 32, wherein the purified immunoglobulin is IgG, or a fragment thereof.
34. The use of claim 33, wherein at least 1%, 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 11%, 12%, 13%, 14%, 15%, 20%, or more of the purified IgG binds to the filovirus glycoprotein.
35. The use of any one of claims 32 to 34, wherein the purified immunoglobulin can prevent or minimize symptoms in a subject infected with a filovirus.

36. The use of any one of claims 31 to 35, wherein the filovirus is MARV, EBOV, SUDV, BDBV, TAFV, or RESTV.

37. The use of any one of claims 31 to 36, wherein the equine is immunized with a mucin-like domain-deleted filovirus spike glycoprotein.

38. The use of any one of claims 31 to 37, wherein the transmembrane domain of the spike glycoprotein is deleted.

39. The use of claim 37 or claim 38, wherein the spike glycoprotein comprises the GP1 subunit or a fragment thereof from MARV, EBOV, SUDV, BDBV, TAFV, RESTV, or a combination of GP1 subunits thereof.

40. The use of claim 37 or claim 38, wherein the spike glycoprotein comprises the GP1 subunit or a fragment thereof and the GP2 subunit or a fragment thereof from MARV, EBOV, SUDV, BDBV, TAFV, RESTV, or a combination of GP1 and GP2 subunits thereof.

41. The use of any one of claims 37 to 40, wherein the spike glycoprotein comprises an amino acid sequence that is at least 90%, at least 95%, or 100% identical to SEQ ID NOS: 2, 4, 6, 8, 10, or 12.

42. The use of any one of claims 37 to 41, wherein the equine is immunized with the spike glycoprotein on days 0, 21, 42, and 63, respectively.

43. The use of claim 41 or claim 42, wherein the polyclonal immunoglobulin is recovered as plasma on day 90 via plasmapheresis.

44. The use of claim 43, wherein the spike glycoprotein comprises MARV GP-ΔTM, and wherein the recovered plasma has an EC<sub>50</sub> titer for binding to MARV GP-ΔTM of at least 10<sup>2</sup>, at least 5 x 10<sup>2</sup>, at least 10<sup>3</sup>, at least 5 x 10<sup>3</sup>, at least 10<sup>4</sup>, at least 5 x 10<sup>4</sup>, at least 10<sup>5</sup>, or at least 5 x 10<sup>5</sup>, as determined by ELISA.

45. The use of claim 43 or claim 44, wherein the spike glycoprotein comprises MARV GP- $\Delta$ TM, and wherein the purified IgG binds to MARV GP- $\Delta$ TM with an EC50 of less than 3  $\mu$ g/ml, less than 2.5  $\mu$ g/ml, less than 2  $\mu$ g/ml, less than 1.5  $\mu$ g/ml, or less than 1  $\mu$ g/ml, or less than 0.5  $\mu$ g/ml, as measured ELISA.

46. The use of any one of claims 43 to 45, wherein two doses of about 100 mg/kg of the immunoglobulin administered to a mouse following a lethal challenge with a filovirus can protect the mouse against the lethal challenge.

47. The use of any one of claims 37 to 41, wherein the equine is immunized in a prime-boost regimen.

48. The use of claim 47, wherein the prime-boost regimen comprises priming with a filovirus VLP and boosting with the spike glycoprotein.

49. The use of claim 48, wherein the VLP comprises a filovirus glycoprotein and a filovirus VP40.

50. The use of claim 49, wherein the VLP further comprises the filovirus nucleoprotein (NP).

51. The use of any one of claims 47 to 50, wherein a prime dose is administered on day zero and day 21, respectively, and a boost dose is administered on day 42 and day 63, respectively.

52. The use of any one of claims 47 to 51, wherein the polyclonal immunoglobulin is recovered as plasma on day 90 via plasmapheresis.

53. The use of claim 51 or claim 52, wherein the prime dose comprises an EBOV VLP comprising GP, VP40, and NP, the boost dose comprises EBOV GP- $\Delta$ Muc, and wherein the recovered plasma has an EC50 titer for binding to EBOV GP- $\Delta$ TM of at least  $10^3$ , at least  $5 \times 10^3$ , at least  $10^4$ , at least  $5 \times 10^4$ , at least  $10^5$ , or at least  $5 \times 10^5$ , as determined by ELISA.

54. The use of claim 51 or claim 52, wherein the prime dose comprises an EBOV VLP comprising GP, VP40, or NP, the boost dose comprises EBOV GP- $\Delta$ Muc, and wherein the purified IgG binds to EBOV GP- $\Delta$ TM or EBOV GP- $\Delta$ Muc with an EC<sub>50</sub> of less than 1  $\mu$ g/ml, less than 0.9  $\mu$ g/ml, less than 0.8  $\mu$ g/ml, less than 0.7  $\mu$ g/ml, less than 0.6  $\mu$ g/ml, less than 0.5  $\mu$ g/ml, less than 0.4  $\mu$ g/ml, less than 0.3  $\mu$ g/ml, less than 0.2  $\mu$ g/ml, less than 0.1  $\mu$ g/ml, or less than 0.09  $\mu$ g/ml, as measured ELISA.

55. The use of any one of claims 47 to 54, wherein two doses of about 100 mg/kg of the immunoglobulin administered to a mouse following a lethal challenge with a filovirus can protect the mouse against the lethal challenge.

56. The use of any one of claims 30 to 55, wherein the filovirus-mediated disease comprises one or more symptoms selected from the group consisting of: fever, internal hemorrhaging, edema, organ failure, headache, malaise, myalgia, nausea, vomiting, bleeding of needle puncture sites, hematemesis, melena, petechiae, ecchymosis, maculopapular rash, disseminated intravascular coagulation, shock, jaundice, conjunctivitis, diarrhea, pharyngitis, convulsions, delirium, coma, oliguria, and epistaxis.

57. The use of any one of claims 31 to 56, wherein the subject is a human.