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(54) Title: HUMANIZED FILOVIRUS ANTIBODIES AND USES THEREOF

(57) Abstract: The present disclosure relates to an antibody or antigen-binding portion thereof that binds to a filovirus. The antibody or antigen-binding portion thereof may have one or more murine CDRs and one or more human framework regions. Also provided herein are compositions comprising the antibody or antigen-binding portion thereof, methods of producing the antibody or antigen-binding portion thereof and methods of using the antibody or antigen-binding portion thereof.



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HUMANIZED FILOVIRUS ANTIBODIES AND USES THEREOF

CROSS-REFERENCE TO RELATED APPLICATIONS

[1001] This application claims priority to U.S. Provisional Application No. 62/118,432, filed February 19, 2015, which is hereby incorporated by reference in its entirety for all purposes.

FIELD OF THE DISCLOSURE

[1002] The present disclosure relates to an antibody or antigen-binding portion thereof that binds to a filovirus, compositions comprising the antibody or antigen-binding portion thereof, methods of producing the antibody or antigen-binding portion thereof and methods of using the antibody or antigen-binding portion thereof.

DESCRIPTION OF THE TEXT FILE SUBMITTED ELECTRONICALLY

[1003] The content of the text file submitted electronically herewith is incorporated herein by reference in its entirety: A computer readable format copy of the Sequence Listing (filename: EMER_051_01WOSeqList_ST25.txt); date recorded: February 19, 2016; file size 140 KB).

BACKGROUND

[1004] Filovirus infections have been associated with severe fatality rates in humans. Filoviruses are enveloped, negative-strand RNA viruses and can cause lethal hemorrhagic fever in humans and non-human primates. The *Filoviridae* family includes the genera *Marburgvirus* and *Ebolavirus*.

[1005] The *Marburgvirus* genus includes the species, *Marburg marburgvirus*, which includes the members Marburg virus (MARV) and Ravn virus (RAVV). There are at least two MARV strains, Musoke and Popp, which were identified when the Ravn virus and Angola virus emerged.

[1006] The *Ebolavirus* (EBOV) is a pleiomorphic filamentous virus in the *Filoviridae* family. Infection with EBOV usually causes a severe hemorrhagic fever, with 50-90% lethality. The outbreak frequency of EBOV has also increased recently. Five different species of EBOV have been identified: Zaire, Sudan, Cote d'Ivoire, Reston and Bundibugyo,

each named after the location in which the species was first described. All species are believed to be lethal to humans, with the possible exception of the rare Cote d'Ivoire species and the Reston species. Of these species, the Zaire species of *Ebolavirus* (ZEBOV) is believed to be the most common and the most lethal.

[1007] The negative-stranded RNA genome of a filovirus encodes seven genes. The proteins encoded by the seven genes include the glycoprotein (GP). The GP is responsible for attached and entry of the virus into target cells and is expressed as a precursor that is cleaved to yield two subunits: GP1, which contains the putative receptor-binding region and heavily glycosylated mucin domain; and GP2, which drives membrane fusion.

[1008] Natural survival from filovirus infection is rare and not clearly understood. There are currently no approved vaccines or therapeutics for filovirus infection. Development of neutralizing antibodies in the context of natural infection is believed to be difficult. Accordingly, there is a need for the development of vaccines and therapeutics for filovirus infection. The present disclosure addresses these needs and provides related advantages.

SUMMARY OF THE DISCLOSURE

[1009] The present disclosure provides an antibody or antigen-binding portion thereof that binds to a filovirus. In some embodiments, the antibody or antigen-binding portion thereof that binds to a filovirus, is an isolated antibody or antigen-binding portion thereof comprising: (a) a light chain CDR1 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NO: 6, 30, 54, 78, 102, 126, 150, 174 or 198; (b) a light chain CDR2 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NO: 7, 31, 55, 79, 103, 127, 151, 175, or 199; (c) a light chain CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NO: 8, 32, 56, 80, 104, 128, 152, 176, or 200; (d) a heavy chain CDR1 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NO: 18, 42, 66, 90, 114, 138, 162, 186, or 210; (e) a heavy chain CDR2 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NO: 19, 43, 67, 91, 115, 139, 163, 187, or 211; (f) a heavy chain CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NO: 20, 44, 68, 92, 116, 140, 164, 188, or 212; (g) a light chain FR1 comprising an amino acid sequence that

has at least about 85% sequence identity to an amino acid sequence e comprising SEQ ID NO: 333, 341, 349, 357, 365, 373, 381, 389, or 397; (h) a light chain FR2 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NO: 334, 342, 350, 358, 366, 374, 382, 390 or 398; (i) a light chain FR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NO: 335, 343, 351, 359, 367, 375, 383, 391 or 399; (j) a light chain FR4 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NO: 336, 344, 352, 360, 368, 376, 384, 392, or 400; (k) a heavy chain FR1 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NOs: 337, 345, 353, 361, 369, 377, 385, 393, or 401; (l) a heavy chain FR2 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NO: 338, 346, 354, 362, 370, 378, 386, 394, or 402; (m) a heavy chain FR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NO: 339, 347, 355, 363, 371, 379, 387, 395 or 403; and, (n) a heavy chain FR4 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NO: 340, 348, 356, 364, 372, 380, 388, 396, or 404.

[1010] In another embodiment, the isolated antibody or antigen-binding portion thereof comprises: (a) a light chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NOs: 6, 7 and 8, respectively; a heavy chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NOs: 18, 19 and 20, respectively; a light chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NOs: 333, 334, 335 and 336, respectively; and a heavy chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NOs: 337, 338, 339, and 340, respectively; (b) a light chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NOs: 30, 31, and 32, respectively; a heavy chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NOs: 42, 43, and 44, respectively; a light chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85% sequence

identity to an amino acid sequence e comprising SEQ ID NOs: 341, 342, 343, and 344, respectively; and a heavy chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NOs: 345, 346, 347, and 348, respectively; (c) a light chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NOs: 54, 55, and 56, respectively; a heavy chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NOs: 66, 67, and 68, respectively; a light chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NOs: 349, 350, 351, and 352, respectively; and a heavy chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NOs: 353, 354, 355, and 356, respectively; (d) a light chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NOs: 78, 79 and 80, respectively; a heavy chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NOs: 90, 91 and 92, respectively; a light chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NOs: 357, 358, 359 and 360, respectively; and a heavy chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NOs: 361, 362, 363, and 364, respectively; (e) a light chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NOs: 102, 103, and 104, respectively; a heavy chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NOs: 114, 115, and 116, respectively; a light chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NOs: 365, 366, 367, and 368, respectively; and a heavy chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NOs: 369, 370, 371, and 372, respectively; (f) a light chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NOs: 126, 127, and 128, respectively; a heavy chain CDR1, CDR2, and CDR3

comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NOs: 138, 139, and 140, respectively; a light chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NOs: 373, 374, 375, and 376, respectively; and a heavy chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NOs: 377, 378, 379, and 380, respectively; (g) a light chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NOs: 150, 151, and 152, respectively; a heavy chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NOs: 162, 163, and 164, respectively; a light chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NOs: 381, 382, 383, and 384, respectively; and a heavy chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NOs: 385, 386, 387 and 388, respectively; (h) a light chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NOs: 174, 175, and 176, respectively; a heavy chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NOs: 186, 187, and 188, respectively; a light chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NOs: 389, 390, 391, and 392, respectively; and a heavy chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NOs: 393, 394, 395, and 396, respectively; or (i) a light chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NOs: 198, 199 and 200, respectively; a heavy chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NOs: 210, 211, and 212, respectively; a light chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NOs: 397, 398, 399, and 400, respectively; and a heavy chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence

that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NOs: 401, 402, 403 and 404, respectively.

[1011] In some embodiments, the antibody or antigen-binding portion thereof that binds to a filovirus, is an isolated antibody or antigen-binding portion thereof comprising: (a) a light chain CDR1 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NO: 3, 27, 51, 75, 99, 123, 147, 171 or 195; (b) a light chain CDR2 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NO: 4, 28, 52, 76, 100, 124, 148, 172, or 196; (c) a light chain CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NO: 5, 29, 53, 77, 101, 125, 149, 173, or 197; (d) a heavy chain CDR1 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NO: 15, 39, 63, 87, 111, 135, 159, 183, or 207; (e) a heavy chain CDR2 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NO: 16, 40, 64, 88, 112, 136, 160, 184, or 208; (f) a heavy chain CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NO: 17, 41, 65, 89, 113, 137, 161, 185 or 209; (g) a light chain FR1 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NO: 9, 33, 57, 81, 105, 129, 153, 177, or 201; (h) a light chain FR2 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NO: 10, 34, 58, 82, 106, 130, 154, 178, or 202; (i) a light chain FR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NO: 11, 35, 59, 83, 107, 131, 155, 179 or 203; (j) a light chain FR4 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NO: 12, 36, 60, 84, 108, 132, 156, 180 or 204; (k) a heavy chain FR1 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NO: 21, 45, 69, 93, 117, 141, 165, 189, or 213; (l) a heavy chain FR2 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NO: 22,

46, 70, 94, 118, 142, 166, 190 or 214; (m) a heavy chain FR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NO: 23, 47, 71, 95, 119, 143, 167, 191 or 215; and, (n) a heavy chain FR4 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NO: 24, 48, 72, 96, 120, 144, 168, 192 or 216.

[1012] In some embodiments, the isolated antibody or antigen-binding portion thereof comprises: (a) a light chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NOs: 3, 4, and 5, respectively; a heavy chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NOs: 15, 16, and 17, respectively; a light chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NOs: 9, 10, 11, and 12, respectively; and a heavy chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NOs: 21, 22, 23, and 24, respectively; (b) a light chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NOs: 27, 28, and 29, respectively; a heavy chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NOs: 39, 40, and 41, respectively; a light chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NOs: 33, 34, 35, and 36, respectively; and a heavy chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NOs: 45, 46, 47 and 48, respectively; (c) a light chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NOs: 51, 52, and 53, respectively; a heavy chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NOs: 63, 64, and 65, respectively; a light chain FR1, FR2, FR3, and FR4 comprising

an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NOs: 57, 58, 59 and 60, respectively; and a heavy chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NOs: 69, 70, 71, and 72, respectively; (d) a light chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NOs: 75, 76, and 77, respectively; a heavy chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NOs: 87, 88, and 89, respectively; a light chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NOs: 81, 82, 83, and 84, respectively; and a heavy chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NOs: 93, 94, 95, and 96, respectively; (e) a light chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NOs: 99, 100, and 101, respectively; a heavy chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NOs: 111, 112, and 113, respectively; a light chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NOs: 105, 106, 107, and 108, respectively; and a heavy chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NOs: 117, 118, 119, and 120, respectively; (f) a light chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NOs: 123, 124 and 125, respectively; a heavy chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NOs: 135, 136, and 137, respectively; a light chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising

SEQ ID NOs: 129, 130, 131, 132, respectively; and a heavy chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NOs: 141, 142, 143, and 144, respectively; (g) a light chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NOs: 147, 148 and 149, respectively; a heavy chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NOs: 159, 160, and 161, respectively; a light chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NOs: 153, 154, 155, and 156, respectively; and a heavy chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NOs: 165, 166, 167, and 168, respectively; (h) a light chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NOs: 171, 172, and 173, respectively; a heavy chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NOs: 183, 184, and 185, respectively; a light chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NOs: 177, 178, 179 and 180, respectively; and a heavy chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NOs: 189, 190, 191, and 192, respectively; or (i) a light chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NOs: 195, 196 and 197, respectively; a heavy chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NOs: 207, 208, and 209, respectively; a light chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NOs: 201, 202, 203 and 204, respectively; and a heavy chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least

about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NOs: 213, 214, 215 and 216, respectively.

[1013] In some embodiments, the antibody or antigen-binding portion thereof comprises: (a) a variable heavy chain comprising an amino acid sequence that has at least about 98% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NO: 13, 37, 61, 85, 109, 133, 157, 181, or 205; and (b) a variable light chain comprising an amino acid sequence that has at least about 98% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NO: 1, 25, 49, 73, 97, 121, 145, 169, or 193. In some embodiments, the antibody or antigen-binding portion thereof comprises: (a) a variable heavy chain comprising an amino acid sequence that has at least about 98% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NO: 13 and a variable light chain comprising an amino acid sequence that has at least about 98% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NO: 1; (b) a variable heavy chain comprising an amino acid sequence that has at least about 98% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NO: 37 and a variable light chain comprising an amino acid sequence that has at least about 98% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NO: 25; (c) a variable heavy chain comprising an amino acid sequence that has at least about 98% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NO: 61 and a variable light chain comprising an amino acid sequence that has at least about 98% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NO: 49; (d) a variable heavy chain comprising an amino acid sequence that has at least about 98% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NO: 85 and a variable light chain comprising an amino acid sequence that has at least about 98% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NO: 73; (e) a variable heavy chain comprising an amino acid sequence that has at least about 98% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NO: 109 and a variable light chain comprising an amino acid sequence that has at least about 98% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NO: 97; (f) a variable heavy chain comprising an amino acid sequence that has at least about 98% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NO: 133 and a variable light chain comprising an amino acid sequence that has at least about 98%

sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NO: 121; (g) a variable heavy chain comprising an amino acid sequence that has at least about 98% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NO: 157 and a variable light chain comprising an amino acid sequence that has at least about 98% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NO: 145; (h) a variable heavy chain comprising an amino acid sequence that has at least about 98% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NO: 181 and a variable light chain comprising an amino acid sequence that has at least about 98% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NO: 169; or (i) a variable heavy chain comprising an amino acid sequence that has at least about 98% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NO: 205 and a variable light chain comprising an amino acid sequence that has at least about 98% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NO: 193.

[1014] In some embodiments, the isolated antibody or antigen-binding portion thereof that binds to a filovirus comprises: (a) a variable heavy chain comprising an amino acid sequence that has at least about 98% sequence identity to SEQ ID NO: 14, 38, 62, 86, 110, 134, 158, 182, or 206; and (b) a variable light chain comprising an amino acid sequence that has at least about 98% sequence identity to SEQ ID NO: 2, 26, 50, 74, 98, 122, 146, 170 or 194. In some embodiments, the isolated antibody or antigen-binding portion thereof comprises: (a) a variable heavy chain comprising an amino acid sequence that has at least about 98% sequence identity to SEQ ID NO: 14 and a variable light chain comprising an amino acid sequence that has at least about 98% sequence identity to SEQ ID NO: 2; (b) a variable heavy chain comprising an amino acid sequence that has at least about 98% sequence identity to SEQ ID NO: 38 and a variable light chain comprising an amino acid sequence that has at least about 98% sequence identity to SEQ ID NO: 26; (c) a variable heavy chain comprising an amino acid sequence that has at least about 98% sequence identity to SEQ ID NO: 62 and a variable light chain comprising an amino acid sequence that has at least about 98% sequence identity to SEQ ID NO: 50; (d) a variable heavy chain comprising an amino acid sequence that has at least about 98% sequence identity to SEQ ID NO: 86 and a variable light chain comprising an amino acid sequence that has at least about 98% sequence identity to SEQ ID NO: 74; (e) a variable heavy chain comprising an amino acid sequence that has at least about 98% sequence identity to SEQ ID NO: 110 and a variable

light chain comprising an amino acid sequence that has at least about 98% sequence identity to SEQ ID NO: 98; (f) a variable heavy chain comprising an amino acid sequence that has at least about 98% sequence identity to SEQ ID NO: 134 and a variable light chain comprising an amino acid sequence that has at least about 98% sequence identity to SEQ ID NO: 122; (g) a variable heavy chain comprising an amino acid sequence that has at least about 98% sequence identity to SEQ ID NO: 158 and a variable light chain comprising an amino acid sequence that has at least about 98% sequence identity to SEQ ID NO: 146; (h) a variable heavy chain comprising an amino acid sequence that has at least about 98% sequence identity to SEQ ID NO: 182 and a variable light chain comprising an amino acid sequence that has at least about 98% sequence identity to SEQ ID NO: 170; or (i) a variable heavy chain comprising an amino acid sequence that has at least about 98% sequence identity to SEQ ID NO: 206 and a variable light chain comprising an amino acid sequence that has at least about 98% sequence identity to SEQ ID NO: 194.

[1015] In yet other embodiments, the isolated antibody or antigen-binding portion thereof comprises: (a) a variable heavy chain comprising an amino acid sequence comprising SEQ ID NO: 14 and a variable light chain comprising an amino acid sequence comprising SEQ ID NO: 2; (b) a variable heavy chain comprising an amino acid sequence comprising SEQ ID NO: 38 and a variable light chain comprising an amino acid sequence comprising SEQ ID NO: 26; (c) a variable heavy chain comprising an amino acid sequence comprising SEQ ID NO: 62 and a variable light chain comprising an amino acid sequence comprising SEQ ID NO: 50; (d) a variable heavy chain comprising an amino acid sequence comprising SEQ ID NO: 86 and a variable light chain comprising an amino acid sequence comprising SEQ ID NO: 74; (e) a variable heavy chain comprising an amino acid sequence comprising SEQ ID NO: 110 and a variable light chain comprising an amino acid sequence comprising SEQ ID NO: 98; (f) a variable heavy chain comprising an amino acid sequence comprising SEQ ID NO: 134 and a variable light chain comprising an amino acid sequence comprising SEQ ID NO: 122; (g) a variable heavy chain comprising an amino acid sequence comprising SEQ ID NO: 158 and a variable light chain comprising an amino acid sequence comprising SEQ ID NO: 146; (h) a variable heavy chain comprising an amino acid sequence comprising SEQ ID NO: 182 and a variable light chain comprising an amino acid sequence comprising SEQ ID NO: 170; or (i) a variable heavy chain comprising an amino acid sequence comprising SEQ ID NO: 206 and a variable light chain comprising an amino acid sequence comprising SEQ ID NO: 194.

[1016] The isolated antibody or antigen-binding portion thereof disclosed herein can be a whole immunoglobulin, an scFv, a Fab fragment, an F(ab')₂, or a disulfide linked Fv.

[1017] In some embodiments, the isolated antibody or antigen-binding portion thereof binds to the GP subunit of a filovirus, e.g., to a GP1 or GP2 subunit. In some embodiments, the antibody or antigen-binding portion thereof binds to the mucin domain of the GP1 subunit or wing domain of the GP2 subunit. The filovirus can be *Ebolavirus* or *Marburgvirus*, such as *Zaire ebolavirus*, *Sudan ebolavirus*, *Reston ebolavirus*, *Tai Forest ebolavirus*, *Cote d'Ivoire ebolavirus*, *Bundibugyo ebolavirus*, *Marburg virus* or *Ravn virus*. In some embodiments, the antibody is cross-reactive to at least two filoviruses.

[1018] Also provided herein is a nucleic acid sequence encoding an antibody or antigen-binding portion thereof disclosed herein. The present disclosure also provides an expression vector comprising a promoter operably linked to a nucleotide sequence disclosed herein, such as a nucleic acid sequence encoding an antibody or antigen-binding portion thereof disclosed herein. In some embodiments, the expression vector comprises a nucleotide sequence with the following sequences: (a) SEQ ID NOs: 3, 4, 5, 9, 10, 11, 12, 15, 16, 17, 21, 22, 23, and 24; (b) SEQ ID NOs: 27, 28, 29, 33, 34, 35, 36, 39, 40, 41, 45, 46, 47, and 48; (c) SEQ ID NOs: 51, 52, 53, 57, 58, 59, 60, 63, 64, 65, 69, 70, 71, and 72; (d) SEQ ID NOs: 75, 76, 77, 81, 82, 83, 84, 87, 88, 89, 93, 94, 95, and 96; (e) SEQ ID NOs: 99, 100, 101, 105, 106, 107, 108, 111, 112, 113, 117, 118, 119, and 120; (f) SEQ ID NOs: 123, 124, 125, 129, 130, 131, 132, 135, 136, 137, 141, 142, 143, and 144; (g) SEQ ID NOs: 147, 148, 149, 153, 154, 155, 156, 159, 160, 161, 165, 166, 167, and 168; (h) SEQ ID NOs: 171, 172, 173, 177, 178, 179, 180, 183, 184, 185, 189, 190, 191, and 192; or (i) SEQ ID NOs: 195, 196, 197, 201, 202, 203, 204, 207, 208, 209, 213, 214, 215 and 216. In some embodiments, the expression vector comprises a nucleotide sequence selected from the group consisting of SEQ ID NOs. 1, 13, 25, 37, 49, 61, 73, 85, 97, 109, 121, 133, 145, 157, 169, 181, 193, or 205. In some embodiments, the expression vector comprises a nucleotide sequence according to SEQ ID NO: 1, 25, 49, 73, 97, 121, 145, 169, or 193. In some embodiments, the expression vector comprises a nucleotide sequence according to SEQ ID NO: 13, 37, 61, 85, 109, 133, 157, 181, or 205. In other embodiments, the expression vector comprises a nucleotide sequence with the following sequences: (a) SEQ ID NOs: 1 and 13; (b) SEQ ID NOs: 25 and 37; (c) SEQ ID NOs: 49 and 61; (d) SEQ ID NOs: 73 and 85; (e) SEQ ID NOs: 97 and 109; (f) SEQ ID NOs: 121 and 133; (g) SEQ ID NOs: 145 and 157; (h) SEQ ID NOs: 169 and 181; or (i) SEQ ID NOs: 193 and 205.

[1019] Also provided herein is a host cell comprising an expression vector disclosed herein. In some embodiments, the cell is a bacterial, eukaryotic or mammalian cell. The cell can be a COS-1, COS-7, HEK293, BHK21, CHO, BSC-1, HepG2, SP2/0, HeLa, myeloma or lymphoma cell.

[1020] The present disclosure also provides a method of producing an antibody or antigen-binding portion thereof that binds to a filovirus disclosed herein. In some embodiments, the method comprises culturing a host cell, such as one disclosed herein, and recovering the antibody or antigen-binding portion thereof.

[1021] The present disclosure also provides compositions comprising an antibody or antigen-binding portion thereof disclosed herein. In some embodiments, the composition is a pharmaceutical composition comprising an antibody or antigen-binding portion thereof. The pharmaceutical composition can further comprise a pharmaceutically acceptable carrier.

[1022] In some embodiments, the composition comprises an antibody or antigen-binding portion thereof disclosed herein and one or more other antibodies or antigen-binding portions thereof. In some embodiments, the one or more other antibodies or antigen-binding portions thereof can bind a protein produced by a virus in the *Filoviridae* family. In some embodiments, the protein is a glycoprotein. The virus can be *Ebolavirus* or *Marburgvirus*. In some embodiments, the virus is *Zaire ebolavirus*, *Sudan ebolavirus*, *Reston ebolavirus*, *Tai Forest ebolavirus*, *Cote d'Ivoire ebolavirus*, *Bundibugyo ebolavirus*, *Marburg virus* or *Ravn virus*. The composition can further comprise a pharmaceutically acceptable carrier.

[1023] Also provided herein are methods comprising administering an antibody or antigen-binding portion disclosed herein. In one embodiment, a method for reducing, treating or preventing a filovirus infection (e.g., a *Marburgvirus* or *Ebolavirus* infection) in a subject in need thereof comprising administering to the subject a therapeutically effective amount of the antibody or antigen-binding portion thereof disclosed herein is provided. In some embodiments, a method for reducing, treating or preventing an filovirus infection (e.g., a *Marburgvirus* or *Ebolavirus* infection) in a subject in need thereof comprises administering to the subject a therapeutically effective amount of a composition disclosed herein. In some embodiments, the subject is a human.

[1024] Methods for detecting a filovirus (e.g., *Marburgvirus* or *Ebolavirus*) in a sample is also provided herein. In some embodiments, the method comprises contacting the sample with an antibody or antigen-binding portion thereof disclosed herein. In some embodiments, the sample is a cell, tissue, or biological fluid from a subject suspected of having or at risk of a filovirus infection.

DETAILED DESCRIPTION

[1025] The present disclosure relates to an antibody or antigen-binding portion thereof that binds to a filovirus, compositions comprising the antibody or antigen-binding portion thereof, methods of producing the antibody or antigen-binding portion thereof and methods of using the antibody or antigen-binding portion thereof, which are described in further detail below.

[1026] The section headings used herein are for organizational purposes only and are not to be construed as limiting the subject matter described. All documents, or portions of documents, cited herein, including but not limited to patents, patent applications, articles, books, and treatises, are hereby expressly incorporated by reference in their entirety for any purpose. In the event that one or more of the incorporated documents or portions of documents define a term that contradicts that term's definition in the application, the definition that appears in this application controls. However, mention of any reference, article, publication, patent, patent publication, and patent application cited herein is not, and should not be taken as an acknowledgment, or any form of suggestion, that they constitute valid prior art or form part of the common general knowledge in any country in the world.

[1027] In the present description, any concentration range, percentage range, ratio range, or integer range is to be understood to include the value of any integer within the recited range and, when appropriate, fractions thereof (such as one tenth and one hundredth of an integer), unless otherwise indicated. As used herein, "about" means $\pm 20\%$ of the indicated range, value, or structure, unless otherwise indicated. It should be understood that the terms "a" and "an" as used herein refer to "one or more" of the enumerated components unless otherwise indicated. The use of the alternative (*e.g.*, "or") should be understood to mean either one, both, or any combination thereof of the alternatives. As used herein, the terms "include" and "comprise" are used synonymously.

[1028] As used herein, "an antibody that binds to a filovirus" is used interchangeably with "an anti-filovirus antibody." An anti-filovirus antibody refers to a monoclonal or recombinant antibody or antibody fragment that binds to a filovirus with specificity. The antibody can be human, humanized or chimeric. An anti-filovirus antibody or antigen-binding portion thereof includes any antibody or substance having a binding domain with the required specificity. Thus, an anti-filovirus antibody or antigen-binding portion thereof includes antibody fragments, derivatives, functional equivalents and homologues of antibodies, humanized antibodies, including any polypeptide comprising an immunoglobulin

binding domain, whether natural or wholly or partially synthetic. Chimeric molecules comprising an immunoglobulin binding domain, or equivalent, fused to another polypeptide are also included. A humanized antibody may be a modified antibody having the variable regions of a non-human, *e.g.*, murine, antibody and the constant region of a human antibody. A humanized antibody may also be a modified antibody having the variable regions of a non-human, *e.g.*, murine, antibody and the framework region(s) of a human antibody. An anti-filovirus antibody includes anti-*Ebolavirus* antibodies and anti-*Marburgvirus* antibodies, in which an anti-*Ebolavirus* antibody refers to a monoclonal or recombinant antibody or antibody fragment that binds to an *Ebolavirus* with specificity and an anti-*Marburgvirus* antibody refers to a monoclonal or recombinant antibody or antibody fragment that binds to a with *Marburgvirus* specificity. An anti-filovirus antibody also includes an antibody that is cross-reactive to an *Ebolavirus* and a *Marburgvirus*.

[1029] As used herein, the term “humanized” refers to a process of making an antibody or immunoglobulin binding proteins and polypeptides derived from a non-human species (*e.g.*, mouse or rat) less immunogenic to humans, while still retaining antigen-binding properties of the original antibody, using genetic engineering techniques. In some embodiments, the binding domain(s) of an antibody or immunoglobulin binding proteins and polypeptides (*e.g.*, light and heavy chain variable regions, Fab, scFv) are humanized. If derived from a non-human source, other regions of the antibody or immunoglobulin binding proteins and polypeptides, such as the hinge region and constant region domains, can also be humanized.

[1030] The terms “light chain variable region” (also referred to as “light chain variable domain” or “VL” or V_L) and “heavy chain variable region” (also referred to as “heavy chain variable domain” or “VH” or V_H) refer to the variable binding region from an antibody light and heavy chain, respectively. The variable binding regions are made up of discrete, well-defined sub-regions known as “complementarity determining regions” (CDRs) and “framework regions” (FRs). In one embodiment, the FRs are humanized. The term “CL” refers to an “immunoglobulin light chain constant region” or a “light chain constant region,” *i.e.*, a constant region from an antibody light chain. The term “CH” refers to an “immunoglobulin heavy chain constant region” or a “heavy chain constant region,” which is further divisible, depending on the antibody isotype into CH1, CH2, and CH3 (IgA, IgD, IgG), or CH1, CH2, CH3, and CH4 domains (IgE, IgM). A “Fab” (fragment antigen binding) is the part of an antibody that binds to antigens and includes the variable region and CH1 domain of the heavy chain linked to the light chain via an inter-chain disulfide bond.

[1031] The six "complementarity determining regions" or "CDRs" present in an antibody antigen-binding domain are short, non-contiguous sequences of amino acids that are specifically positioned to form the binding domain as the antibody assumes its three dimensional configuration in an aqueous environment. The remainder of the amino acids in the binding domain, referred to as "framework" regions, show less inter-molecular variability. The framework regions largely adopt a β -sheet conformation and the CDRs form loops which connect, and in some cases form part of, the β -sheet structure. Thus, framework regions act to form a scaffold that provides for positioning the CDRs in correct orientation by inter-chain, non-covalent interactions. The binding domain formed by the positioned CDRs defines a surface complementary to the epitope on the immunoreactive antigen. This complementary surface promotes the non-covalent binding of the antibody to its cognate epitope. The amino acids that make up the CDRs and the framework regions, respectively, can be readily identified for any given heavy or light chain variable region by one of ordinary skill in the art, since they have been defined in various different ways (see, "Sequences of Proteins of Immunological Interest," Kabat, E., et al., U.S. Department of Health and Human Services, (1983); and Chothia and Lesk, J. Mol. Biol., 196:901-917 (1987), which are incorporated herein by reference in their entireties). In some embodiments, an antibody, or antigen-binding fragment thereof, contains at least one heavy chain variable region and/or at least one light chain variable region. The heavy chain variable region (or light chain variable region) typically contains three CDRs and four framework regions (FRs), arranged from amino-terminus to carboxyl-terminus in the following order: FR1, CDR1, FR2, CDR2, FR3, CDR3, FR4.

[1032] In the case where there are two or more definitions of a term which is used and/or accepted within the art, the definition of the term as used herein is intended to include all such meanings unless explicitly stated to the contrary. A specific example is the use of the term "complementarity determining region" ("CDR") to describe the non-contiguous antigen combining sites found within the variable region of both heavy and light chain polypeptides. These particular regions have been described, for example, by Kabat et al., U.S. Dept. of Health and Human Services, "Sequences of Proteins of Immunological Interest" (1983) and by Chothia et al., J. Mol. Biol. 196:901-917 (1987), which are incorporated herein by reference. The Kabat and Chothia definitions include overlapping or subsets of amino acids when compared against each other. Nevertheless, application of either definition (or other definitions known to those of ordinary skill in the art) to refer to a CDR of an antibody or variant thereof is intended to be within the scope of the term as defined and used herein,

unless otherwise indicated. The appropriate amino acids which encompass the CDRs as defined by each of the above cited references are set forth below in Table 1 as a comparison. The exact amino acid numbers which encompass a particular CDR will vary depending on the sequence and size of the CDR. Those skilled in the art can routinely determine which amino acids comprise a particular CDR given the variable region amino acid sequence of the antibody.

Table 1: CDR Definitions*

	Kabat	Chothia
VH CDR1	31-35	26-32
VH CDR2	50-65	52-58
VH CDR3	95-102	95-102
VL CDR1	24-34	26-32
VL CDR2	50-56	50-52
VL CDR3	89-97	91-96

*Numbering of all CDR definitions in Table 1 is according to the numbering conventions set forth by Kabat et al. (see below).

[1033] CDRs can also be determined using IMGT® (the international ImMunoGeneTics information system®) numbering. H: heavy chain; K: kappa or L: light chain. Kabat et al. also defined a numbering system for variable domain sequences that is applicable to any antibody. One of ordinary skill in the art can unambiguously assign this system of "Kabat numbering" to any variable domain sequence, without reliance on any experimental data beyond the sequence itself. As used herein, "Kabat numbering" refers to the numbering system set forth by Kabat et al., U.S. Dept. of Health and Human Services, "Sequence of Proteins of Immunological Interest" (1983). Unless use of the Kabat numbering system is explicitly noted, however, consecutive numbering is used for all amino acid sequences in this disclosure.

[1034] As used herein, the term "antigen-binding portion," "antigen-binding region" "or antigen-binding domain" refers to the domain, region, portion, or site of a protein, polypeptide, oligopeptide, or peptide or antibody or binding domain derived from an antibody that possesses the ability to specifically recognize and bind to an antigen. Exemplary binding

antigen-binding portions include single-chain antibody variable regions (e.g., domain antibodies, sFv, scFv, scFab). In certain embodiments, the binding domain comprises or consists of an antigen binding site (e.g., comprising a variable heavy chain sequence and variable light chain sequence or three light chain complementary determining regions (CDRs) and three heavy chain CDRs from an antibody placed into alternative framework regions (FRs) (e.g., human FRs optionally comprising one or more amino acid substitutions). A variety of assays are known for identifying binding domains of the present disclosure that specifically bind a particular target, including Western blot, ELISA, phage display library screening, and BIAcore® interaction analysis.

[1035] An antibody or antigen-binding portion “specifically binds” an antigen if it binds the antigen with an affinity or K_a (i.e., an equilibrium association constant of a particular binding interaction with units of $1/M$) equal to or greater than $10^5 M^{-1}$, while not significantly binding other components present in a test sample. The antibody or antigen-binding portion can be classified as “high affinity” or “low affinity.” “High affinity” refer to those antibodies or antigen-binding portions with a K_a of at least about $10^7 M^{-1}$, at least about $10^8 M^{-1}$, at least about $10^9 M^{-1}$, at least about $10^{10} M^{-1}$, at least about $10^{11} M^{-1}$, at least about $10^{12} M^{-1}$, or at least about $10^{13} M^{-1}$. “Low affinity” refer to those antibodies or antigen-binding portions with a K_a of up to $10^7 M^{-1}$, up to $10^6 M^{-1}$, up to $10^5 M^{-1}$. Alternatively, affinity can be defined as an equilibrium dissociation constant (K_d) of a particular binding interaction with units of M (e.g., $10^{-5} M$ to $10^{-13} M$). Affinities of refer to those antibodies or antigen-binding portions according to the present disclosure can be readily determined using conventional techniques (see, e.g., Scatchard et al. (1949) Ann. N.Y. Acad. Sci. 51:660; and U.S. Patent Nos. 5,283,173, 5,468,614, or the equivalent).

[1036] As used herein, “reference antibody” refers to an antibody that is known in the art and which serves the basis for a humanized, chimeric or recombinant antibody. The reference antibody may be a non-human, (e.g., murine), human, humanized, chimeric and / or recombinant antibody or antibody-like polypeptide.

[1037] “Treatment” or “treating” refers to either a therapeutic treatment or prophylactic/preventative treatment. A therapeutic treatment may improve at least one symptom of disease in an individual receiving treatment or may delay worsening of a progressive disease in an individual, or prevent onset of additional associated diseases.

[1038] Ameliorating or reducing or reduction of infection), as used herein, can include but is not limited to delaying the onset of the infection, attenuating the symptoms of the infection, shortening the duration of the infection, reducing the viral titer in a patient (e.g., in

the blood), or slowing the progression of the infection. Filovirus infections encompassed by the present application include, but are not limited to, *Marburgvirus* and *Ebolavirus*.

[1039] A “therapeutically effective amount,” “therapeutically effective dose” or “effective dose” refers to that amount of the antibody or compound sufficient to result in amelioration of one or more symptoms of the disease being treated. When applied to an individual active ingredient, administered alone, a therapeutically effective dose refers to that ingredient alone. When applied to a combination, a therapeutically effective dose refers to combined amounts of the active ingredients that result in the therapeutic effect, whether administered serially or simultaneously. One or more specific therapeutic molecules may be administered according to methods of the invention, each in an effective dose. The effective dose can be determined empirically through dose studies. The term “therapeutically effective amount” is used interchangeably with “prophylactically effective amount” herein, and refers to an amount that prevents infection with a filovirus, prevents disease associated with a filovirus infection, reduces the number and/or severity of symptoms of a filovirus infection, stops or limits the spread of a filovirus, and/or shortens the duration of a filovirus infection.

[1040] As used herein, the term “pharmaceutically acceptable” refers to molecular entities and compositions that do not generally produce allergic or other serious adverse reactions when administered using routes well known in the art. Molecular entities and compositions approved by a regulatory agency of the Federal or a state government or listed in the U.S. Pharmacopeia or other generally recognized pharmacopeia for use in animals, and more particularly in humans are considered to be “pharmaceutically acceptable.”

[1041] As used herein, the terms “nucleic acid,” “nucleic acid molecule,” or “polynucleotide” refer to deoxyribonucleotides or ribonucleotides and polymers thereof in either single- or double-stranded form. Unless specifically limited, the terms encompass nucleic acids containing analogues of natural nucleotides that have similar binding properties as the reference nucleic acid and are metabolized in a manner similar to naturally occurring nucleotides. Unless otherwise indicated, a particular nucleic acid sequence also implicitly encompasses conservatively modified variants thereof (*e.g.*, degenerate codon substitutions) and complementary sequences as well as the sequence explicitly indicated. Specifically, degenerate codon substitutions can be achieved by generating sequences in which the third position of one or more selected (or all) codons is substituted with mixed-base and/or deoxyinosine residues (Batzer *et al.* (1991) *Nucleic Acid Res.* 19:5081; Ohtsuka *et al.* (1985) *J. Biol. Chem.* 260:2605-2608; Cassol *et al.* (1992); Rossolini *et al.* (1994) *Mol. Cell. Probes* 8:91-98). The term nucleic acid is used interchangeably with gene, cDNA, and mRNA

encoded by a gene. As used herein, the terms "nucleic acid," "nucleic acid molecule," or "polynucleotide" are intended to include DNA molecules (*e.g.*, cDNA or genomic DNA), RNA molecules (*e.g.*, mRNA), analogs of the DNA or RNA generated using nucleotide analogs, and derivatives, fragments and homologs thereof.

[1042] The term "expression vector," as used herein, refers to a nucleic acid molecule, linear or circular, comprising one or more expression units. In addition to one or more expression units, an expression vector can also include additional nucleic acid segments such as, for example, one or more origins of replication or one or more selectable markers. Expression vectors are generally derived from plasmid or viral DNA, or can contain elements of both.

[1043] As used herein, the term "sequence identity" refers to a relationship between two or more polynucleotide sequences or between two or more polypeptide sequences. When a position in one sequence is occupied by the same nucleic acid base or amino acid residue in the corresponding position of the comparator sequence, the sequences are said to be "identical" at that position. The percentage "sequence identity" is calculated by determining the number of positions at which the identical nucleic acid base or amino acid residue occurs in both sequences to yield the number of "identical" positions. The number of "identical" positions is then divided by the total number of positions in the comparison window and multiplied by 100 to yield the percentage of "sequence identity." Percentage of "sequence identity" is determined by comparing two optimally aligned sequences over a comparison window. The comparison window for nucleic acid sequences can be, for instance, at least about 20, 30, 40, 50, 60, 70, 80, 90, 100, 110, 120, 130, 140, 150, 160, 170, 180, 190, 200, 300, 400, 500, 600, 700, 800, 900 or 1000 or more nucleic acids in length. The comparison window for polypeptide sequences can be, for instance, at least about 20, 30, 40, 50, 60, 70, 80, 90, 100, 110, 120, 130, 140, 150, 160, 170, 180, 190, 200, 300 or more amino acids in length. In order to optimally align sequences for comparison, the portion of a polynucleotide or polypeptide sequence in the comparison window can comprise additions or deletions termed gaps while the reference sequence is kept constant. An optimal alignment is that alignment which, even with gaps, produces the greatest possible number of "identical" positions between the reference and comparator sequences. Percentage "sequence identity" between two sequences can be determined using the version of the program "BLAST 2 Sequences" which was available from the National Center for Biotechnology Information as of September 1, 2004, which program incorporates the programs BLASTN (for nucleotide sequence comparison) and BLASTP (for polypeptide sequence comparison), which programs

are based on the algorithm of Karlin and Altschul (Proc. Natl. Acad. Sci. USA 90(12):5873-5877, 1993). When utilizing "BLAST 2 Sequences," parameters that were default parameters as of September 1, 2004, can be used for word size (3), open gap penalty (11), extension gap penalty (1), gap dropoff (50), expect value (10) and any other required parameter including but not limited to matrix option. Two nucleotide or amino acid sequences are considered to have "substantially similar sequence identity" or "substantial sequence identity" if the two sequences have at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 96%, at least about 97%, at least about 98%, or at least about 99% sequence identity relative to each other.

[1044] The present disclosure relates to an antibody or antigen-binding portion thereof that binds to a filovirus, compositions comprising the antibody or antigen-binding portion thereof, methods of producing the antibody or antigen-binding portion thereof and methods of using the antibody or antigen-binding portion thereof.

[1045] The terms "antibody that binds to a filovirus" and "anti-filovirus antibody" are used interchangeably herein. Examples of an anti-filovirus antibody or antigen-binding portion thereof, include, but are not limited to, (i) the Fab fragment consisting of VL, VH, CL and CH domains; (ii) the Fd fragment consisting of the VH and CH domains; (iii) the Fv fragment consisting of the VL and VH domains of a single antibody (e.g., linked by a disulfide bond); (iv) the dAb fragment (Ward, E. S. et al., Nature 341: 544-546 (1989)) which consists of a VH domain; (v) isolated CDR regions; (vi) F(ab')₂ a bivalent fragment comprising two linked Fab fragments; (vii) single chain Fv molecules (scFv), wherein a VH domain and a VL domain are linked by a peptide linker which allows the two domains to associate to form an antigen binding site (Bird et al., Science 242: 423-426 (1988); Huston et al., PNAS USA 85: 5879-5883 (1988)); (viii) bispecific single chain Fv dimers (PCT/US92/09965); (ix) "diabodies", multivalent or multispecific fragments constructed by gene fusion (WO94/13804; P. Hollinger et al., Proc. Natl. Acad. Sci. USA 90: 6444-6448 (1993)); and (x) whole immunoglobulin.

[1046] In one embodiment, an "anti-filovirus antibody" is a recombinant anti-filovirus antibody or polypeptide. Recombinant anti-filovirus antibodies and polypeptides include, for instance, Fc fusions, toxin fusions, fusions to enzymatic activities, minibodies, diabodies, linear antibodies, single chain antibodies, bispecific antibody fragments, scFv and Fab fragments. A recombinant anti-filovirus antibody includes a molecule or polypeptide that incorporates an amino acid sequence derived from an anti-filovirus antibody and which is capable of binding a filovirus with specificity. Recombinant anti-filovirus antibodies include

molecules that are optimized, for instance, for stability, solubility, *in vitro* and *in vivo* binding.

[1047] In one embodiment, an anti-filovirus antibody is a diabody. Diabodies are multimers of polypeptides, each polypeptide comprising a first domain comprising a binding region of an immunoglobulin light chain and a second domain comprising a binding region of an immunoglobulin heavy chain, the two domains being linked (*e.g.*, by a peptide linker) but unable to associated with each other to form an antigen binding site: antigen binding sites are formed by the association of the first domain of one polypeptide within the multimer with the second domain of another polypeptide within the multimer. See WO94/13804 which is incorporated by reference in its entirety.

[1048] In one embodiment, an anti-filovirus antibody is a scFv. A scFv is constructed by joining a variable heavy chain and a variable light chain with a linker using recombinant methods. The linker that enables the V_H and V_L regions to be made as a single chain protein. See, for instance, Bird *et al.*, 1988, *Science* 242:423-426 and Huston *et al.*, 1988, *Proc. Natl. Acad. Sci. USA* 85:5879-5883. In one embodiment, the scFv comprises V_H and V_L regions that are identical or derived from a reference anti-filovirus antibody.

[1049] In one embodiment, an anti-filovirus antibody or antigen-binding portion thereof is an Fv. An Fv is an antibody fragment which contains a complete antigen-recognition and binding site. This region consists of a dimer of one heavy and one light chain variable domain in tight, non-covalent or covalent association. It is in this configuration that the three CDRs of each variable domain interact to define an antigen-binding site on the surface of the V_H-V_L dimer. Collectively, the six CDRs confer antigen-binding specificity to the antibody. However, even a single variable domain (or half of an Fv comprising only three CDRs specific for an antigen) has the ability to recognize and bind antigen, although at a lower affinity than the entire binding site. In one embodiment, the Fv comprises V_H and V_L regions that are identical or derived from a reference anti-filovirus antibody.

[1050] In one embodiment of the invention, an anti-filovirus antibody is a single chain polypeptide comprising, from amino to carboxyl terminus, a binding domain (*e.g.*, scFv), an immunoglobulin hinge region and an immunoglobulin constant region. In this embodiment, also known as a small modular immunopharmaceutical (SMIP), the single chain polypeptide forms a dimer in solution.

[1051] The anti-filovirus antibody or antigen-binding portion thereof can be a recombinant polypeptide, fusion protein or immunoconjugate that binds a filovirus and comprise an antibody fragment or are derived in part from a monoclonal or polyclonal anti-

filovirus antibody. In some embodiments, an anti-filovirus antibody or antigen-binding portion thereof is a molecule or polypeptide that is derived from a reference anti-filovirus antibody and is capable of binding with specificity to the same epitope as the reference anti-filovirus antibody. In some embodiments, the epitope is on a GP subunit of a filovirus, e.g., a GP1 or GP2 subunit. Thus, in one embodiment, the anti-filovirus antibody or antigen-binding portion thereof binds to the GP1 or GP2 subunit of the filovirus. In some embodiments, the anti-filovirus antibody or antigen-binding portion thereof binds to the mucin domain of the GP1 subunit or the wing domain of the GP2 subunit. The GP subunit can be from *Ebolavirus* or *Marburgvirus*, such as *Zaire ebolavirus*, *Sudan ebolavirus*, *Reston ebolavirus*, *Tai Forest ebolavirus*, *Cote d'Ivoire ebolavirus*, *Bundibugyo ebolavirus*, *Marburg virus* or *Ravn virus*.

[1052] In some embodiments, the anti-filovirus antibody binds to one or more species of *Ebolavirus*. In some embodiments, the anti-filovirus antibody binds to *Marburg virus* or *Ravn virus*. In some embodiments, the anti-filovirus antibody binds to at least two filoviruses. In some embodiments, the anti-filovirus antibody binds to an *Ebolavirus* or *Marburgvirus*.

[1053] An anti-filovirus derived from a reference anti-filovirus antibody can include a molecule or polypeptide comprising at least about 10 contiguous amino acids, at least about 20 contiguous amino acids or at least about 50 or more contiguous amino acids as the reference anti-filovirus antibody.

[1054] In one embodiment, an anti-filovirus antibody or antigen-binding portion thereof comprises a heavy chain CDR1, heavy chain CDR2, heavy chain CDR3, light chain CDR1, light chain CDR2, and/or light chain CDR3 with the same amino acid sequence as a reference anti-filovirus antibody. In another embodiment, an anti-filovirus antibody or antigen-binding portion thereof comprises a heavy chain CDR1, heavy chain CDR2, heavy chain CDR3, light chain CDR1, light chain CDR2, and/or light chain CDR3 that has an amino acid sequence comprising a sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to an amino acid sequence of the respective heavy chain CDR1, heavy chain CDR2, heavy chain CDR3, light chain CDR1, light chain CDR2, and/or light chain CDR3 of a reference anti-filovirus antibody or molecule.

[1055] In another embodiment, an anti-filovirus antibody or antigen-binding portion thereof comprises a VH and/or VL with the same amino acid sequence as a reference anti-filovirus molecule. In another embodiment, an anti-filovirus antibody or antigen-binding portion thereof comprises a VH and/or VL that has an amino acid sequence comprising a

sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to an amino acid sequence of the respective VH and/or VL of a reference anti-filovirus molecule.

[1056] In some embodiments, the reference anti-filovirus molecule is a murine anti-filovirus antibody. In some embodiments, the reference anti-filovirus molecule is a murine anti-Marburgvirus antibody. In one embodiment, the reference anti-filovirus molecule is the murine anti-filovirus antibody CAN30G5, CAN54G2, CAN30G2, CAN40G1, CAN30G1, CAN30G3, or CAN30G4. The CDRs, VHs and VLs of these murine antibodies are provided in Table 2.

Table 2

Name	Chain, Region	Origin	Sequence	SEQ ID NO:
huCAN30G5	K, Variable region	Artificial sequence	gacatcgigtgaccagtcceccctgtccctgcccgtgacctgggcca gcccgcctccatctcctgccgtctctccagtcctgggtgacctcaacg gcaacacctacctgcaactgtaccagcagcgcccggccagtcceccc gectgctgatetacaagggtgtccaaccgcttccggcggtgcccgaecgc ttctccggctccggctccggcaccgacttcacctgaagatctcccggt ggaggcggaggagcgtggcggtgtactactgtccagtcacccacgtg ccctggaccttcggcgccggcaccagggtggagatcaagc	1
huCAN30G5	K, variable region	Artificial sequence	DIVLTQSPLSLPVTILGQPASISCRSSQSLVHSNG NTYLHWYQQRPGQSPRLLIYKVSNNRFSGVDPDR FSGSGSGTDFTLKISRVEAEDVGVVYCSQSSTHV PWTFGGGTKVEIK	2
huCAN30G5	K, CDR1	Artificial sequence	cagtcctctgggtgacctccaacggcaacacctac	3
huCAN30G5	K, CDR2	Artificial sequence	aaggtgtcc	4
huCAN30G5	K, CDR3	Artificial sequence	tccagtcacccacgtgcccgtggacc	5
huCAN30G5	K, CDR1	Artificial sequence	QSLVIHSNGNTY	6
huCAN30G5	K, CDR2	Artificial sequence	KVS	7
huCAN30G5	K, CDR3	Artificial sequence	SQSTIHPWT	8
huCAN30G5	K, FR1	Artificial sequence	gacatcgigtgaccagtcceccctgtccctgcccgtgacctgggcca gcccgcctccatctcctgccgtctctcc	9
huCAN30G5	K, FR2	Artificial sequence	ctgcaactgglaaccagcagcgcccggccagtccecccgcctgctgatct ac	10
huCAN30G5	K, FR3	Artificial sequence	aaccgcttctccggcggtgcccgaecgcttctccggcctccggcga ccgacttcacctgaagatctccggcggtggaggccgaggacgtggcggt gtactactgc	11
huCAN30G5	K, FR4	Artificial sequence	ttcgccggcgccgcaaccaagggtggagatcaagc	12
huCAN30G5	L, Variable region	Artificial sequence	gaggtgcagctgggtggagtccggcggcgccctgggtgagcccggcgg ctccctgaagctgtctgtccgcctccggcttgccttcaactctacgc catgcaactgggtgcccagccctccgcaaggccctggagtggtggc ccgcatccgcatcaagtcgggaactacgccacctctacgccggtctc gtgaaggccgcttaccctgtcccgacpactccaggaacacctteta	13

			cctgcagatgaactccctgaagaccgaggacaccgccaatgtactactgc gtgcgcgagtggaggaggcgccatggactactggggccagggcaccct ggtgaccgtgtctctccg	
huCAN30G5	II, variable region	Artificial sequence	EVQLVESGGGLVQPGGSLKLSCAASGFAFNSY AMIIWVRQASGKGLEWVARIRIKSGNYATSYA GSVKGRFTVSRDDSKNTFYLMNSLKTEDTA MYCYCVREWEGAMDYWGQGTLVTVSS	14
huCAN30G5	H, CDR1	Artificial sequence	ggcttgccttcaactctacgcc	15
huCAN30G5	II, CDR2	Artificial sequence	atccgcataagtcgcgcaactacgccacc	16
huCAN30G5	II, CDR3	Artificial sequence	gtgcgcgagtggaggaggcgccatggactac	17
huCAN30G5	H, CDR1	Artificial sequence	GFAFNSYA	18
huCAN30G5	II, CDR2	Artificial sequence	IRIKSGNYAT	19
huCAN30G5	II, CDR3	Artificial sequence	VREWEGAMDY	20
huCAN30G5	II, FR1	Artificial sequence	gagggtgcagctgggtggagtcggcgccggccctgggtgcagccggcgcc ctccctgaagctgtctgcgcgcctcc	21
huCAN30G5	II, FR2	Artificial sequence	atgcactgggtgcgcgcagccctccggcgaaggccctggagtggtgccc cgc	22
huCAN30G5	H, FR3	Artificial sequence	tctacgcgcggctccgtgaaggccgcttcaccgtgtccgcgcgacgaact ccaagaacacctctactctgcagatgaactccctgaagaccgaggacac cgccatgtactactgc	23
huCAN30G5	II, FR4	Artificial sequence	tggggccagggcaccctgggtgaccgtgtctctccg	24
rehuCAN30G5	K, Variable region	Artificial sequence	gacatcgtgctgaaccagtcceccctgtccctgcccgtagccctgggcca gcccgcctccatctcctgccgtctccagtcctgggtgcactccaacg gcaaacctacactgcactggtaacctgcagaagcccgccagtccecccg cctgctgatctacaaggtgtccaaccgtctccggcgtgcccgaaccgtt ctccggctccggctccggcaccgacttcacctgaagatctcccgctg gaggccgaggacgtggggcgtgtactctgtctccagtcacccacgtgc cctggacctcggcgccggcaccacagctggagatcaag	25
rehuCAN30G5	K, variable region	Artificial sequence	DIVLTQSPSLSPVTLGQPASISCRSSQSLVHSNG NTYLIWYLOKPGQSPRLIYKVSNRFSGVPDR FSGSGSGTDFTLKISRVEAEDVGVYFCSQSTII PWTFGGGTKLEIK	26
rehuCAN30G5	K, CDR1	Artificial sequence	cagtcctgggtgcactccaacggcaacactac	27
rehuCAN30G5	K, CDR2	Artificial sequence	aagggtgccc	28
rehuCAN30G5	K, CDR3	Artificial sequence	tcccagtcacccacgtgcccctggacc	29
rehuCAN30G5	K, CDR1	Artificial sequence	QSLVHSNGNTY	30
rehuCAN30G5	K, CDR2	Artificial sequence	KVS	31
rehuCAN30G5	K, CDR3	Artificial sequence	SQSTIIHPWT	32
rehuCAN30G5	K, FR1	Artificial sequence	gacatcgtgctgaaccagtcceccctgtccctgcccgtagccctgggcca gcccgcctccatctcctgccgtctctcc	33
rehuCAN30G5	K, FR2	Artificial sequence	ctgcactggtaacctgcagaagcccgccagtccecccgccctgctgatcia c	34
rehuCAN30G5	K, FR3	Artificial sequence	naaccgttctccggcgtgcccgaccgcttccggctccggcctccggca ccgacttcacctgaagatctcccgctggaggccgaggacgtggcgct	35

			gtactctgc	
rehuCAN30G5	K, FR4	Artificial sequence	ttcggcggcgccaccacgaagctggagatcaag	36
rehuCAN30G5	II, Variable region	Artificial sequence	gaggtgcagctgggtggagtcggcgccggcgccctgggtgcagcccggcgcc ctccctgaagctgtctcgcgcgcctccggcctgggttcgcttcaactcctacgc catgcactgggtgtgtccaggcctccggcaaggcctggagtgggtggc ccgcacccgcacaaagtcggcaactacgccacctcctacgccggctcc gtgaaggccgcttcaccgtgtcccggaagacacccaagtcctgttcta cctgcagatgaacaacctgaagaccgaggacaccgccatgtactactgc gtgcgcgagtgaggaggcgccatggactactggggccaggccacct ggtgacctgtcctcc	37
rehuCAN30G5	H, variable region	Artificial sequence	EVQLVESGGGLVQPGGSLKLSCAASGFAFNSY AMHWVCQASGKGLEWVARIRIKSGNYATSYA GSVKGRFTVSRDDSKSLFYLMNLTEDTA MYVCVREWEGAMDYWGQGTLVTVSS	38
rehuCAN30G5	II, CDR1	Artificial sequence	ggcttcgcttcaactcctacgcc	39
rehuCAN30G5	H, CDR2	Artificial sequence	atccgcataagtcggcaactacgccacc	40
rehuCAN30G5	II, CDR3	Artificial sequence	gtgcgcgagtgaggaggcgccatggactac	41
rehuCAN30G5	II, CDR1	Artificial sequence	GFAFNSYA	42
rehuCAN30G5	II, CDR2	Artificial sequence	IRIKSGNYAT	43
rehuCAN30G5	II, CDR3	Artificial sequence	VREWEGAMDY	44
rehuCAN30G5	II, FR1	Artificial sequence	gaggtgcagctgggtggagtcggcgccggcgccctgggtgcagcccggcgcc ctccctgaagctgtctcgcgcgcctcc	45
rehuCAN30G5	II, FR2	Artificial sequence	atgcactgggtgtgtccaggcctccggcaaggcgctggagtgggtggcc cgc	46
rehuCAN30G5	H, FR3	Artificial sequence	tcctacgccggctcctgaaggccgcttcacctgtcccgcgacgaact ccaagtccctgttctacctgcagatgaacaacctgaagaccgaggacac cgccatgtactactgc	47
rehuCAN30G5	II, FR4	Artificial sequence	tggggccaggcgaccctgggtgacctgtcctcc	48
cdrCAN30G5	K, Variable region	Artificial sequence	gacgtggtgatgaccagtcctccctgtccctgcccgtgacctgggcc agcccgcctccatcctcgcgcctcctccagtcctgtgtgactccaac ggcaacacctacctgaactgggtccagcagcgccccggcagtcctccc gcccctgactacaaagggtccaaccgcgactccggcggtgccgaccg ctctccggctccggctccggcaccgacttcacctgaagatctcccgcg tggaggccgaggacgtggcggtgtactactgtccagtcacccacgt gcccgtgaccttcggcgccggcaccacgaaggtggagatcaag	49
cdrCAN30G5	K, variable region	Artificial sequence	DVVMTQSPPLSLPVTLGQPASISCRSSQSLVHSN GNTYLNWFQQRPGQSPRRLIYKVSNRDSGVPD RFGSGSGTDFTLKISRVEAEDVGVYYCSQSTH VPWTFGGGTKVEIK	50
cdrCAN30G5	K, CDR1	Artificial sequence	cagtcctcgtgactccaacggcaacactac	51
cdrCAN30G5	K, CDR2	Artificial sequence	aaggtgtcc	52
cdrCAN30G5	K, CDR3	Artificial sequence	tcccagtcacccaagtgccttgacc	53
cdrCAN30G5	K, CDR1	Artificial sequence	QSLVHSNGNTY	54
cdrCAN30G5	K, CDR2	Artificial sequence	KVS	55
cdrCAN30G5	K, CDR3	Artificial sequence	SQSTHVPWT	56

cdrCAN30G5	K, FR1	Artificial sequence	gaegtggtagaccagacccccctgccccgtgacccgtgggccc agcccgccctccatccctgcccctctcc	57
cdrCAN30G5	K, FR2	Artificial sequence	ctgaactgggtccagcagcgcgcgcgcagtcccccccgcgcctgatct ac	58
cdrCAN30G5	K, FR3	Artificial sequence	aaccgcgactccggcggtgccgaccgcttctccggctccggctccggca ccgacttcacccctgaagatctcccggtggagggccgaggacgtggggcgt gtactactgc	59
cdrCAN30G5	K, FR4	Artificial sequence	ttcgccggcgccaccaagggtggagatcaag	60
cdrCAN30G5	H, Variable region	Artificial sequence	gagggtgcagctgggtggagtcggcgccggcctgggtgcagccggcg ctccctgaagctgtcttgcgcgcgcctccggcttcgcttcaactctacgc catgcactgggtgcgcagggcctccggcaaggccctggagtggtggg ccgcatccgcatcaagtcggcnaactacgccaccgctacgcgcctcc gtgaaggggccgcttaccatctcccgagcactccaagaacacgcct acctgcagatgaactccctgaagaccgagggacacccgcgtgtactactg cgtgcgcgagtgggagggcgccatggactactggggccagggcaccc tggtagccgtgtctcc	61
cdrCAN30G5	H, variable region	Artificial sequence	EVQLVESGGGLVQPGGSLKLSCAASGFAFNSY AMHWVRQASGKGLEWVGRIRIKSGNYATAYA ASVKGRFTISRDDSKNTAYLQMNSLKTEDTAV YYCVREWEGAMDYWGQGTLLTVSS	62
cdrCAN30G5	H, CDR1	Artificial sequence	ggcttgccttcaactctacgcc	63
cdrCAN30G5	H, CDR2	Artificial sequence	atccgcataaagtcgcgcaactacgccacc	64
cdrCAN30G5	H, CDR3	Artificial sequence	gtgcgcgagtgggagggcgccatggactac	65
cdrCAN30G5	H, CDR1	Artificial sequence	GFAFNSYA	66
cdrCAN30G5	H, CDR2	Artificial sequence	IRIKSGNYAT	67
cdrCAN30G5	H, CDR3	Artificial sequence	VREWEGAMDY	68
cdrCAN30G5	H, FR1	Artificial sequence	gaggtgcagctgggtggagtcggcgccggcctgggtgcagccggcg ctccctgaagctgtcttgcgcgcgcctcc	69
cdrCAN30G5	H, FR2	Artificial sequence	atgcactgggtgcgcagggcctccggcaaggccctggagtggtgggc cgc	70
cdrCAN30G5	H, FR3	Artificial sequence	gcctacgccgcctccgtgaaggggcgttaccatctccgcgacgaet ccaagaacaccgctaccctgcagatgaactccctgaagaccgaggaca ccgccgtgtactactgc	71
cdrCAN30G5	H, FR4	Artificial sequence	tggggccagggcaccctggtagccgtgtctcc	72
huCAN40G1	K, Variable region	Artificial sequence	gacatcgltgaccaglcceccgcctccctggccgtglectggcg agcgcgccaccatctctgcaaggcctccagtcctggaccacgacg ggactctacatgaactggtagcagcagaagcccgccagccccc agctgctgactacgccacctcaacctggagtcggcatcccccccg cttctccggctccggctccggcaccgacttaccctgaccatctctccct gcaggccgaggacgtggccacctactactgcagcagtcctacgaggt gcccctgaccttcggcgccggcaccagctggagatcaagc	73
huCAN40G1	K, variable region	Artificial sequence	DIVLTQSPASLAVSLGERATISCKASQSVSDHDG DSYMNWYQQKPGQPPKLLIYATSNLESGLPAR FSGSGSGTDFTLTISSLQAEDVATYYCQQSYEV PLTFGAGTKLEIK	74
huCAN40G1	K, CDR1	Artificial sequence	cagtcctggaccacgacggcgactctac	75
huCAN40G1	K, CDR2	Artificial sequence	gccacctcc	76
huCAN40G1	K, CDR3	Artificial sequence	cagcagtcctacgaggtgcccctgacc	77

huCAN40G1	K, CDR1	Artificial sequence	QSV DHDGDSY	78
huCAN40G1	K, CDR2	Artificial sequence	ATS	79
huCAN40G1	K, CDR3	Artificial sequence	QQSYEVPLT	80
huCAN40G1	K, FR1	Artificial sequence	gacatcgtgctgaccagtcctcccgctccctggccgtgtccctggggc agegcgcaccatctcctgcaaggcctcc	81
huCAN40G1	K, FR2	Artificial sequence	atgaactggtagcagcagaagcccgccagcccccaagctgctgatct ac	82
huCAN40G1	K, FR3	Artificial sequence	aacctggagtcggcagtcctcccgctctccgggtccggctccggca ccgacttcacctgaccatctcctccctgcaaggccgaggacgtggccac ctactactgc	83
huCAN40G1	K, FR4	Artificial sequence	tteggcgccggcaccnaagctggagatcaagc	84
huCAN40G1	H, Variable region	Artificial sequence	gagggtgcagctgcagcagtcggccccgagggtgaagaagcccggcgc ctccgtgaagggtgtcctgccgcacctccggctacaccltaccgagtaca ccatccactgggtgaagcagggccccggcaaggccctggagtgatcg ggcgatcaaccccaaccacggcgccacctgtacaaccagaagtca aggggccgcgtgacctgacctgtggacaagtcctctccaccgctacat ggagctgtcccgctgctccgacgacaccggcgtgtactactgcgcc cgttcaactacgactactggggccaggcaccctgggtgacctgtctcc cg	85
huCAN40G1	II, variable region	Artificial sequence	EVQLQQSGPEVKKPGASVKVSCRTSGYTFTEY THIHWVKQAPGKGLEWIGGINPNIIIGGTLNQKF KGRVTLTVDKSSSTAYMELSLRSDDTAVYYC ARFTYDYWGQGLTVTVSS	86
huCAN40G1	II, CDR1	Artificial sequence	ggctacacettaccaggtacacc	87
huCAN40G1	H, CDR2	Artificial sequence	atcaaccccaaccacggcgccacc	88
huCAN40G1	II, CDR3	Artificial sequence	ggcgcttaccctacgactac	89
huCAN40G1	H, CDR1	Artificial sequence	GYTFTEYT	90
huCAN40G1	II, CDR2	Artificial sequence	INPNIIIGGT	91
huCAN40G1	H, CDR3	Artificial sequence	ARFTYDY	92
huCAN40G1	H, FR1	Artificial sequence	gagggtgcagctgcagcagtcggccccgagggtgaagaagcccggcgc ctccgtgaagggtgtcctggcgacctcc	93
huCAN40G1	II, FR2	Artificial sequence	atccactgggtgaagcagggccccggcaaggccctggagtggatcggc ggc	94
huCAN40G1	H, FR3	Artificial sequence	ctgtacaaccagaagtcaaggcgccgtgacctgacctgtggacaagt ctctctccaccgctacatggagctgtcccgctgcgciccgacgacac cgccgtgtactactgc	95
huCAN40G1	II, FR4	Artificial sequence	tggggccagggcaccctgggtgacctgtctcccg	96
rehuCAN40G1	K, Variable region	Artificial sequence	gacatcgtgctgaccagtcctcccgctccctggccgtgtccctggggc agegcgcaccatctcctgcaaggcctccagtcctgtggaccacgacg ggactctacatgaactgtaccagcagaagcccgccagccccca agctgtgatctacgccacctcaacctggagtccggcatccccggcg ctctccggctccggctccggcaccgacttaccctgaacatctctccgt gcaggccgaggacgtggccacctactactgcagcagtcctacagggt gcccctgaacttcggcgcccgccaccaagctggagctgaag	97

rehuCAN40G1	K, variable region	Artificial sequence	DIVLTQSPASLAVSLGERATISCKASQSVDDHDG DSYMNWYQQKPGQPPKLLIYATSNLESGIPAR FSGSGSGTDFTLNISVVQAEDVATYYCQQSYEV PLTFGAGTKLELK	98
rehuCAN40G1	K, CDR1	Artificial sequence	cagtcctgtgaccacgacggcgactctac	99
rehuCAN40G1	K, CDR2	Artificial sequence	gcacacctcc	100
rehuCAN40G1	K, CDR3	Artificial sequence	cagcagtcctacgaggtgccccgacc	101
rehuCAN40G1	K, CDR1	Artificial sequence	QSVDIIDGDSY	102
rehuCAN40G1	K, CDR2	Artificial sequence	ATS	103
rehuCAN40G1	K, CDR3	Artificial sequence	QQSYEVPLT	104
rehuCAN40G1	K, FR1	Artificial sequence	gacatcgtgctgaccagtcctcccgctccctggccgtgacctggggc agcgcgcacacctctctgcaaggctcc	105
rehuCAN40G1	K, FR2	Artificial sequence	atgaactggtagcagcagaagcccgccagcccccaagctgctgatc ac	106
rehuCAN40G1	K, FR3	Artificial sequence	aacctggagtcggcagcctcccgctctccggctccggctccggca ccgacttcacctgaacatctctcgtgcaggccgaggacgtggccac ctactactgc	107
rehuCAN40G1	K, FR4	Artificial sequence	ttcggcgccggcaccgaagctggagctgaag	108
rehuCAN40G1	II, Variable region	Artificial sequence	gaggtgcagctgcagcagtcggccccgaggtgggaagcccggcgc ctccgtgaagatctctgcgcacctccggctacacctcaccagtlaca ccatccatcgggtgaagcaggccccggcaaggccctggagtgatcg ggggcatcaaccccaaccacggcgccacctgtacaaccagaagtca aggcccgcccaacctgacctgggacagtcctctccaccgctacai ggagctgccccgctgcgctccgacgacacccgctgtaactacgcgc cgcttcacctagactactggggccaggcaccctgctgacctgtctctc c	109
rehuCAN40G1	H, variable region	Artificial sequence	EVQLQQSGPEVVKPGASVKISCRISGYTFTEYT IIWVVKQAPGKGLEWIGGINPNHIGGTLYNQKF KGRATLTVDKSSSTAYMELSLRSDDTAVYYC ARFTYDYWGQGTLLTVSS	110
rehuCAN40G1	II, CDR1	Artificial sequence	ggctacaccttcaccagtlacacc	111
rehuCAN40G1	H, CDR2	Artificial sequence	atcaacccaaccaaggcgccacc	112
rehuCAN40G1	H, CDR3	Artificial sequence	ggcgcttcacctagactac	113
rehuCAN40G1	II, CDR1	Artificial sequence	GYTFTEYT	114
rehuCAN40G1	H, CDR2	Artificial sequence	INPNHGGT	115
rehuCAN40G1	II, CDR3	Artificial sequence	ARFTYDY	116
rehuCAN40G1	H, FR1	Artificial sequence	gaggtgcagctgcagcagtcggccccgaggtgggaagcccggcgc ctccgtgaagatctctgcgcacctcc	117
rehuCAN40G1	II, FR2	Artificial sequence	atccactgggtgaagcaggccccggcaaggccctggagtgatcggc ggc	118
rehuCAN40G1	II, FR3	Artificial sequence	ctgtacaaccagaagtcaaggcccgccaccctgacctgggacaagi cctctccaccgctacatggagctgtccgctgcgctccgacgacac cgccgtgtaactactgc	119
rehuCAN40G1	II, FR4	Artificial	tggggccaggcgaccctgctgacctgtctctcc	120

		sequence	
cdrCAN40G1	K, Variable region	Artificial sequence gacatcgtgatgaccacagtcctcccgactccctggccgtgtccctgggcg agcgcgccaccatcaactgcaagtcctccagtcctggaccacgacg gcgactcciaactggcctgglaaccagcagaagcccgccagccccc agetgtgatctacgcaccccccaccccgagtcctggcgtgcccgaccg cttctccggctccggctccggcaccgacttcaacctgaccatctctccct gcaggccgaggacgtggcctgtactactgccagcagtcctacgaggt gcccctgaecttcggccaaggcaccagctggagatcaag	121
cdrCAN40G1	K, variable region	Artificial sequence DIVMTQSPDSLAVSLGERATINCKSSQSVDIIDG DSYLAWYQQKPGQPPKLLIYATSTRESGV PDR FSGSGSGTDFTLTISSLQAEDVAVYYCQQSYEV PLTFGQGTKLEIK	122
cdrCAN40G1	K, CDR1	Artificial sequence cagtcctgtggaccacgacggcgactcctac	123
cdrCAN40G1	K, CDR2	Artificial sequence gccacctcc	124
cdrCAN40G1	K, CDR3	Artificial sequence cagcagtcctacgaggtgcccctgacc	125
cdrCAN40G1	K, CDR1	Artificial sequence QSVDIIDGDSY	126
cdrCAN40G1	K, CDR2	Artificial sequence ATS	127
cdrCAN40G1	K, CDR3	Artificial sequence QQSYEVPLT	128
cdrCAN40G1	K, FR1	Artificial sequence gacatcgtgatgaccacagtcctcccgactccctggccgtgtccctgggcg agcgcgccaccatcaactgcaagtcctcc	129
cdrCAN40G1	K, FR2	Artificial sequence ctggcctgtgaccagcagaagcccgccagcccccagctgtgatct ac	130
cdrCAN40G1	K, FR3	Artificial sequence accgcggagtcctggcgtgcccgaaccgtctctccggctccggctccggc accgacttcaacctgaacctctctccctgcaggccgaggacgtggcctg gtactactgc	131
cdrCAN40G1	K, FR4	Artificial sequence ttcggccaggccaccagctggagatcaag	132
cdrCAN40G1	II, Variable region	Artificial sequence caggtgcagctggtgcagtcggcgccgaggtgaagaagcccggcgc ctccgtgaaggtgtcctgcaaggcctccggctacacettaccgagtaca ccaatgcactgggtgcccagggcccccggccagggtgctggagtgatg ggctggatcaaccccaaccacggcgccaccactacgccagaaagttc caggggccgctgaccatgacccggcgaacctccatctccaccgacctaca tggagctgtcccgctgctccgacgacaccgcccgtgtactactgcgc ccgcttcaactacgactactggggccaggccacctggtagccgtglect cc	133
cdrCAN40G1	H, variable region	Artificial sequence QVQLVQSGAEVKKPGASVKVSCKASGYTFTE YTMIIWVRQAPGQGLEWMGWINPNIIGGTNY AQKFQGRVTMTTRDTSISTAYMELSR LRSDDTA VYYCARFTYDYWGQGLTVTVSS	134
cdrCAN40G1	II, CDR1	Artificial sequence ggctacaccttaccgagtagacc	135
cdrCAN40G1	II, CDR2	Artificial sequence atcaaccccaaccacggcgccacc	136
cdrCAN40G1	H, CDR3	Artificial sequence gcccgttccactacgactac	137
cdrCAN40G1	II, CDR1	Artificial sequence GYTFTEYT	138
cdrCAN40G1	H, CDR2	Artificial sequence INPNHGGT	139
cdrCAN40G1	H, CDR3	Artificial sequence ARFTYDY	140
cdrCAN40G1	II, FR1	Artificial sequence caggtgcagctggtgcagtcggcgccgaggtgaagaagcccggcgc ctccgtgaaggtgtcctgcaaggcctcc	141

cdrCAN40G1	H, FR2	Artificial sequence	atgcactgggtgcgcagggcccccggccagggcctggagtgatgggctgg	142
cdrCAN40G1	II, FR3	Artificial sequence	aactacgcccagaaagttccaggggcgcgtgacctgacccgcgacacc tccalcaccacggcctacalggagctgltccgcctgcgtccgacgacac cgccgtgtaactatgc	143
cdrCAN40G1	II, FR4	Artificial sequence	tggggccaggggcaccctgggtgacctgtgctctcc	144
huCAN54G2	K, Variable region	Artificial sequence	gacgtgggtgatgacccagacccccctgacctgcccgtgacctggggc agcccgccctccatctctgcacctcccccagtcctgtgaactccgac ggcgagacctacctgaaciggtgtctgcagcgccecgccaglccecc aagcgccctgatccacctgggtgccaaagctggactccggcggtgcccgacc gcttctccggctccggctccggcaccgacttccctgaagatctcccg gtggaggccgaggagctggggcgtgtactactgtggcaggggcaccac ttccccctggaccttcggcgggcgccaccaagggtggagatcaagc	145
huCAN54G2	K, variable region	Artificial sequence	DVVMYQTPLTLPTLGPASISCTSSQSLLNSD GETYLNWLLQRPQSPKRLIHLVSKLDSGVPD RFSGSGSGTDFTLKISRVEAEDVGVVYCWQGT III'PWT'FGGGTKVEIK	146
huCAN54G2	K, CDR1	Artificial sequence	cagtcctctgctgaactccgacggcgagacctac	147
huCAN54G2	K, CDR2	Artificial sequence	ctgggtgcc	148
huCAN54G2	K, CDR3	Artificial sequence	tggcaggggcaccacactccccctggacc	149
huCAN54G2	K, CDR1	Artificial sequence	QSLNNSDGETY	150
huCAN54G2	K, CDR2	Artificial sequence	LVS	151
huCAN54G2	K, CDR3	Artificial sequence	WQGTHTFPWT	152
huCAN54G2	K, FR1	Artificial sequence	gacgtgggtgatgacccagacccccctgacctgcccgtgacctggggc agcccgccctccatctctgcacctccccc	153
huCAN54G2	K, FR2	Artificial sequence	ctgaactggctgctgcagcgccecgccagtccecccaagcgctgatcc ac	154
huCAN54G2	K, FR3	Artificial sequence	aagctggactccggcggtgcccgaccgcttctccggctccggctccggca ccgacttccacctgaagatctcccgctggaggccgaggacgtgggggt gtactactgc	155
huCAN54G2	K, FR4	Artificial sequence	ttccggcgggcgccaccaagggtggagatcaagc	156
huCAN54G2	II, Variable region	Artificial sequence	cagggtgcagctgcagcagtcggcgaccgaggtgaagaagcccgggc ctccgtgaaggtgtcctgcaaggcctccggctacgacttccacactctg gctgggctggatccgccaggcccccgccagggcctggatggatcg gcgacalcaccccgggcggaacacccactacaacgagaagtcaa ggcgccggtgacctgaccgcccgaagtcctccacacccgctatcat ggagctgtctccctgcgtccgaggacaccgctgtacttctgtctcat gatcctgtacaccctggactactggggccaggggcaccctgggtgaccgtg tccctccg	157
huCAN54G2	II, variable region	Artificial sequence	QVQLQQSGTEVKKPGASVKVSKASGYDTN FWLGWIRQAPGQGLEWIGDIYPGGDNTYYNE KFKGRVTLTADKSSNTAYMELSSLRSEDVAVY FCFMILYTLDYWGQGLTVTVSS	158
huCAN54G2	II, CDR1	Artificial sequence	ggctacgacttccaccaactctgg	159
huCAN54G2	II, CDR2	Artificial sequence	atctacccgggcgggcacaacacc	160
huCAN54G2	H, CDR3	Artificial sequence	ttcatgatectgtacacctggactac	161
huCAN54G2	II, CDR1	Artificial sequence	GYDFTNFW	162

huCAN54G2	H, CDR2	Artificial sequence	IYPGGDNT	163
huCAN54G2	II, CDR3	Artificial sequence	FMILYTLDY	164
huCAN54G2	H, FR1	Artificial sequence	cagggtgcagctgcagcagtcggcaccgaggtgaagaagcccggcgcctccgtgaaggtgtccctgcaaggccctcc	165
huCAN54G2	H, FR2	Artificial sequence	ctgggctggatccgccaggcccccgccaggccctggagtggatcggcgac	166
huCAN54G2	II, FR3	Artificial sequence	tactacaacagagaagticaaggcccgctgacctgaccgcccagacaagtcctcaacacccgctacatggagctgtccctccctgcgctccgaggacacggccgtgtacttctgc	167
huCAN54G2	H, FR4	Artificial sequence	tggggccaggcgaccctgggtgacctgtgtccctcg	168
rehuCAN54G2	K, Variable region	Artificial sequence	gaegtggtgatgaccagacccccctgacctgcccgtgacctggggcageccgctccatctcctgcacctcctccagtcctgtgaactccgacggcgagacctacctgaactggctgtgcagcgccccggccagtcctccaaagcgcctgatccactgtgtgctcnaagctggactccggcggtcccgaccgcatctccggctccggctccggcaccgacitcaccctgaagatctccgcgtgcaggccgaggacctggcgatctactactgtgcaggggcaccacttcccttgaccttcggcgccggcaccgaaggtggagatcnaag	169
rehuCAN54G2	K, variable region	Artificial sequence	DVVMTQTPLTLPTLGPASISCTSSQSLLNSDGETYLNWLLQRPQSPKRLIHLVSKLDSGVPRISGSGSGTDFTLKISRVEAEDLGIYYCWQGTII FPWTFGGGKVEIK	170
rehuCAN54G2	K, CDR1	Artificial sequence	cagtcctgtgtaactccgacggcgagacctac	171
rehuCAN54G2	K, CDR2	Artificial sequence	ctgggtgcc	172
rehuCAN54G2	K, CDR3	Artificial sequence	tggcaggcgacccacttccctggacc	173
rehuCAN54G2	K, CDR1	Artificial sequence	QSLLNSDGETY	174
rehuCAN54G2	K, CDR2	Artificial sequence	LVS	175
rehuCAN54G2	K, CDR3	Artificial sequence	WQGTII FPWT	176
rehuCAN54G2	K, FR1	Artificial sequence	gacgtgggtgagaccagacccccctgacctgcccgtgacctggggcageccgctccatctcctgcacctccctcc	177
rehuCAN54G2	K, FR2	Artificial sequence	ctgaactggctgtgcagcgccccggccagtcctcccaagcgctgacctac	178
rehuCAN54G2	K, FR3	Artificial sequence	aagctggactccggcggtcccgaccgcatctccggctccggctccggcaccgactcaccctgaagatctcccgctggaggccgaggacctgggc atctactactgc	179
rehuCAN54G2	K, FR4	Artificial sequence	tccggcgccggcaccgaaggtggagatcaag	180
rehuCAN54G2	II, Variable region	Artificial sequence	cagggtgcagctgcagcagtcggcaccgaggtgggaagccccggcgccctccgtgaagatctccgcaaggcctccggctacgacttcccaactctgtgtgggtggatcaagcaggccccggccaggccctggagtgatcgggacatctacccccggcgccgacaacacctactacaacgagaagttcaagggaaggtgacctgaccggcgacaagtcctccaaacacccgctacatggagttctccctccctgcgctccgaggacaccggcggtgtacttctgttcatgacctgtacacctggactactggggccaggcgaccctggtgacctgtgtctcc	181
rehuCAN54G2	II, variable region	Artificial sequence	QVQLQQSGTEVVKPGASVKISCKASGYDFTNFWLGWIKQAPGQGLEWIGDIYPGGDNTYYNEKFKGKVTLTADKSSNTAYMEFSSLRSEDTAVYFCFMILYTLDYWGQGLVTVSS	182
rehuCAN54G2	II, CDR1	Artificial sequence	ggctacgacttcccaacttctgg	183

		sequence		
rehuCAN54G2	II, CDR2	Artificial sequence	atctacccccggcggcgacaaace	184
rehuCAN54G2	II, CDR3	Artificial sequence	ttcatgatccgtacacccctggactac	185
rehuCAN54G2	II, CDR1	Artificial sequence	GYDFTNFW	186
rehuCAN54G2	II, CDR2	Artificial sequence	IYPGGDNT	187
rehuCAN54G2	H, CDR3	Artificial sequence	FMILYTLDY	188
rehuCAN54G2	II, FR1	Artificial sequence	caggatgcagctgcagcagtcgggcaccgaggtggtgaagcccggcgc ctccgtgaagatctcttgcaggcctcc	189
rehuCAN54G2	H, FR2	Artificial sequence	ctgggctggatcaagcaggccccggccaggcctggagtggatcgg cgac	190
rehuCAN54G2	II, FR3	Artificial sequence	tactacaacgagaagttcaagggaaggtgacccctgaccgcgcgacaa cctccaaacaccgcctacatggagtctccctccctggctccgaggacacc ggcgtgtactctgc	191
rehuCAN54G2	II, FR4	Artificial sequence	tggggccagggcaccctgggtgaccgtgtctcc	192
cdrCAN54G2	K, Variable region	Artificial sequence	gacgtggtgatgacccagtcccccctgtccctgcccgtgacctgggccc agcccgctccatctctcgcgcctccctccagtcctgctgaactcgcac ggcgagacctaccctgaactggttccagcagcgcgccggcagtcctccc cgccgcctgatctacctgtgttccaaccgcgactccggcgtgcccagcc gcttctcggctccggctccggcaccgacttaccctgaagatctccgc gtggaggccgaggacgtgggcgtgtactactgtgtggcagggaacccac ttccctggaceltcggcgccgcacccaagggtggagatcaag	193
cdrCAN54G2	K, variable region	Artificial sequence	DVVMTQSPLSLPVTLGQPASISCRSSQSLLNSD GETYLNWFQQRPGQSPRRLLIYLVSNRDSGVDP RFSGSGSGTIDFTLKISRVEAEDVGVVYCWQGT IIFPWTFGGGTKVEIK	194
cdrCAN54G2	K, CDR1	Artificial sequence	cagtcctctgctgaactcgcagcgcgagacctac	195
cdrCAN54G2	K, CDR2	Artificial sequence	ctggtgtcc	196
cdrCAN54G2	K, CDR3	Artificial sequence	tggcaggcgccacccaacttccccggacc	197
cdrCAN54G2	K, CDR1	Artificial sequence	QSLLNSDGETY	198
cdrCAN54G2	K, CDR2	Artificial sequence	LVS	199
cdrCAN54G2	K, CDR3	Artificial sequence	WQGTHTFPWT	200
cdrCAN54G2	K, FR1	Artificial sequence	gacgtggtgatgacccagtcccccctgtccctgcccgtgacctgggccc agcccgctccatctctcgcgcctccctcc	201
cdrCAN54G2	K, FR2	Artificial sequence	ctgaactgggtccagcagcgccccggccagtcccccggcgctgatct ac	202
cdrCAN54G2	K, FR3	Artificial sequence	aaccgggactcggcggtgcccgaccgcttctcggctccggctccggca ccgacttaccctgaagatctcccggtggaggccgaggacgtggcggt gtactactgc	203
cdrCAN54G2	K, FR4	Artificial sequence	ttcgccggcgccaccaagggtggagatcaag	204
cdrCAN54G2	H, Variable region	Artificial sequence	caggatgcagctgggtgcagtcggcgccgaggtgaagaagcccggcgc ctccgtgaagggtgtctgcaaggcctccggctacgaacttcaacaactctg gatgcactgggtgcgcaggccccggccaggcctggagtggagtg gcatcatctacccggcgcgacaacacctctacgccagaaagtcca gggcgcggtgacctgacccggcacacctccacctccacctgtacatg gagctgtctccctgcgctccgaggacaccgocgtgtactactgtctcatg atcctgtacacctggactactggggccagggcacctgggtgacctgtgc	205

			ctcc	
cdrCAN54G2	II, variable region	Artificial sequence	QVQLVQSGAEVKKPGASVKVSKASGYDFTN FWMIIWVRQAPGQGLEWMGHIYPGGDNTSYA QKFQGRVTMTTRDTSTSTVYMELSSLRSEDTAV YYCFMILYTLDYWGQGTLVTVSS	206
cdrCAN54G2	II, CDR1	Artificial sequence	gggtacgacttcaccaactctctgg	207
cdrCAN54G2	II, CDR2	Artificial sequence	atctaccceggcgcgcgacacacacc	208
cdrCAN54G2	II, CDR3	Artificial sequence	ttcatgacctgtacacctggactac	209
cdrCAN54G2	H, CDR1	Artificial sequence	GYDFTNFW	210
cdrCAN54G2	II, CDR2	Artificial sequence	IYPGGDNT	211
cdrCAN54G2	II, CDR3	Artificial sequence	FMILYTLDY	212
cdrCAN54G2	II, FR1	Artificial sequence	caggtgcagctgggtgcagtcggcgccgaggtgaagaagcccggegc ctccgtgaaggtgtcttgcgaaggcctcc	213
cdrCAN54G2	II, FR2	Artificial sequence	atgcactgggtgcgcagggcccccggccagggcctggagtgatggg catc	214
cdrCAN54G2	H, FR3	Artificial sequence	tctacgccagaaagttccagggcgcggtgacctgacctgcgcacacct ccacctccacctgtacatggagctgtctcctgcgcctccgagacacc ggcgtgtactactgc	215
cdrCAN54G2	II, FR4	Artificial sequence	tggggccagggcacccctgggtgacctgtctctcc	216
Ravn GPeAmuc	GPeAmuc ATM	Synthetic Marburg virus	MKTIYFLISL ILIQSIKTLV VLEIASNSQP QDVDSVCSGT LQKTEDVHLM GFTLSGQKVA DSPLEASKRW AFRTGVPPKN VEYTEGEEAK TCYNISVTDP SGKSLLLDPP SNIRDYPKCK TVHHIQGQNP HAQGIALHLW GAFFLYDRVA STTMYRGKVF TEGNIAAMIV NKTVHRMIFS RQGQGYRHMN LTSTNKYWTS SNETQRNDTG CFGILQEYNS TNNQTCPPSL KPPSLPTVTP SIHSTNTQIN TAKSGTMRPP IYFRKKRSIF WKEGDIFPFL DGLINTEIDF DPIPNTETIF DESPSFNTST NEEQHTPPNI SLTFSYFPDK NGDTAYSGEN ENDCDAELRI WSVQEDDLAA GLSWIPFFGP GIEGLYTAGL IKNNQNNLVCR LRRLANQTAK SLELLLRVTT EERTFSLINR HAIDFLLTRW GGTCKVLGPD CCIGIEDLSK NISEQIDKIR KDEQKEET	217
Angola GPeAmuc	GPeAmuc ATM	Synthetic Marburg virus	MKTTCLLISL ILIQGVKTLV ILEIASNIQP QNVDSVCSGT LQKTEDVHLM GFTLSGQKVA DSPLEASKRW AFRAGVPPKN VEYTEGEEAK TCYNISVTDP SGKSLLLDPP TNIRDYPKCK TIIHHIQGQNP IIAQGIALHLW GAFFLYDRVA STTMYRGKVF TEGNIAAMIV NKTVIKMFIS RQGQGYRIHMN LTSTNKYWTS SNGTQNTDGT CFGTLQEYNS TKNQTCAPSK KPLPLPTAIP EVKLTTSTSD ATKLNNTQHL VYFRKRKNIL WREGDMFPFL DGLINAPIDF DPVPTKTIF DESSSSGASA EEDQIIASPNI SLTFSYFPKV NENTAHSNGEN ENDCDAELRI WSVQEDDLAA GLSWIPFFGP GIEGLYTAGL IKNNQNNLVCR	218

			LRRLANQTAK SLELLLRVTT EERTFSLINR HAIDFLLARW GGTCCKVLGPD CCIGIEDLSR NISEQIDQIK KDEQKEGT	
Musoke GPeΔmuc	GPeΔmuc ΔTM	Synthetic Marburg virus	MKTTCLFISL ILIQGTKNLP ILEIASNNQP QNVDSVCSGT LQKTEDVILM GFTLSGQKVA DSPLEASKRW AFRTGVPPKN VEYTEGEEAK TCYNISVTDP SGKSLLLDPP TNIRDYPKCK TIIIIHQGQNP IIAQGIALIILW GAFFLYDRIA STTMYRGKVF TEGNIAAMIV NKTVIIKMIFS RQGQGYRIHMN LTSTNKYWTS SNGTQTNDTG CFGALQEYNS TKNQTCAPSK IPPPLPTARP EIKLTSTPTD ATKLNNTQIIL VYFRRKRSIL WREGDMFPFL DGLINAPIDF DPVPNTKTIF DESSSSGASA EEDQIIASPNI SLTLSYFPNI NENTAYSGEN ENDCDAELRI WSVQEDDLAA GLSWIPFFGP GIEGLYTAVL IKNQNNLVCR LRRLANQTAK SLELLLRVTT EERTFSLINR HAIDFLLTRW GGTCCKVLGPD CCIGIEDLSK NISEQIDQIK KDEQKEGT	219
Ci67 GPeΔmuc	GPeΔmuc ΔTM	Synthetic Marburg virus	MKTTCLFISL ILIQGIKTLF ILEIASNNQP QNVDSVCSGT LQKTEDVILM GFTLSGQKVA DSPLEASKRW AFRTGVPPKN VEYTEGEEAK TCYNISVTDP SGKSLLLDPP TNIRDYPKCK TIIIIHQGQNP IIAQGIALIILW GAFFLYDRIA STTMYRGRVF TEGNIAAMIV NKTVIIKMIFS RQGQGYRIHMN LTSTNKYWTS NNGTQTNDTG CFGALQEYNS TKNQTCAPSK IPSPLPTARP EIKPTSTPTD ATTLNNTQIIL VYFRKKRSIL WREGDMFPFL DGLINAPIDF DPVPNTKTIF DESSSSGASA EEDQIIASPNI SLTLSYFPNI NENTAYSGEN ENDCDAELRI WSVQEDDLAA GLSWIPFFGP GIEGLYTAGL IKNQNNLVCR LRRLANQTAK SLELLLRVTT EERTFSLINR HAIDFLLTRW GGTCCKVLGPD CCIGIEDLSR NISEQIDQIK KDEQKEGT	220
CAN30G5	K, Variable region	Murine sequence	gataitgtgtgacccaatctccactctccctgctgtcagtttggagatc aagcctccatctcttcagatctagtcagagcctgtacacagtaattggaa acacettattacatttgtaactgcagaagccagggcagctetccaaacctcc tgatctacnaagttccaaccgattttctgggtccagacaggttcagtg cagtggaatcagggacagatttcacactcaagatcagcagagtgagggt gaggatctgggagttatttctgcctcnaaglacacatgttccgtggacgt cggtggaggcaccagctggaaatcaaa	221
CAN30G5	K, variable region	Murine sequence	DIVLTQSPLSLPVSLGDQASISCRSSQSLVIISNG NTYLIWYLQKPGQSPNLLIYKVSNRFSQVPDR FSGSGSGTDFTLKISRVEAEDLGVYFCSQSTIIV PWTFGGGKLEIK	222
CAN30G5	K, CDR1	Murine sequence	cagagcctgtacacagtaattggaacacctat	223
CAN30G5	K, CDR2	Murine sequence	aaagttcc	224
CAN30G5	K, CDR3	Murine sequence	tctcaagtacacatgttccgtggacg	225
CAN30G5	K, CDR1	Murine sequence	QSLVIISNGNTY	226
CAN30G5	K, CDR2	Murine sequence	KVS	227

CAN30G5	K, CDR3	Murine sequence	SQSTHVPWT	228
CAN30G5	II, Variable region	Murine sequence	gagggtgcagcctgttgagictggaggattgggcagccaaaggatc attgaactctcatgtgccgcctcgtgttcgcctcaattcclatgccatgc actgggtctgccaggctccaggaaagggttgggaatgggtgtctgcata agaatlaaaagtggaattatgcaacatctatgccgggtcagtgacagaca gattcaccgtctccagagatgattcacaaaactgttctatctgcaaatgaa caacctgaaaactgaggacacagccatgtattactgtgtgagagagtggg aaggggtatggactactgggtgcaaggaaacctcagtcaccgtctctca g	229
CAN30G5	II, variable region	Murine sequence	EVQLVESGGGLVQPKGSLKLSCAASGFAFNSY AMHWVCQAPGKGLEWVARIRIKSGNYATSYA GSVTDRTVSRDDSQLFLYLQMNNLKTEDTA MYYCVREWEGAMDYWGQGTSTVTVSS	230
CAN30G5	II, CDR1	Murine sequence	ggtttgccttcaattctatgcc	231
CAN30G5	II, CDR2	Murine sequence	ataagaattaaagtggaattatgcaaca	232
CAN30G5	H, CDR3	Murine sequence	gtgagagagtgggaagggtatggactac	233
CAN30G5	II, CDR1	Murine sequence	GFAFNSYA	234
CAN30G5	II, CDR2	Murine sequence	IRIKSGNYAT	235
CAN30G5	II, CDR3	Murine sequence	VREWEGAMDY	236
CAN54G2	K, Variable region	Murine sequence	gatgtgtgatgaccagactccctcactttgtcgggtaccattggacagc cagccctcatctcttgcacgtcaagtcagagcctcttaaatagtgtatggg agacatatttgaattggtgttacagagccagggccagtcctcaaaagcgc taatccatctgtgtctaaactggactctggagtcctgacaggaactg gcagtggaatctgggacagatttcacactgaaatcaacagagtggaggct gaggattgggaatttatattgtctggcaaggatcacatttccgtggacgtt cgggtggaggccaccaagctggaaatcaaac	237
CAN54G2	K, variable region	Murine sequence	DVVMITQPLTLSTVIGQPASISCTSSQSLLNSDG ETYNWLLQRPQGSPKRLIHLVSKLDSGVPDRI TGSGSGTDFTLKINRVEAEDLGIYYCWQGTIIF PWTFGGGTKLEIK	238
CAN54G2	K, CDR1	Murine sequence	cagagccctctaaatagtgtatggggagacatat	239
CAN54G2	K, CDR2	Murine sequence	ctgggtgtct	240
CAN54G2	K, CDR3	Murine sequence	tggcaagggtacacatttccgtggagc	241
CAN54G2	K, CDR1	Murine sequence	QSLLNSDGETY	242
CAN54G2	K, CDR2	Murine sequence	LVS	243
CAN54G2	K, CDR3	Murine sequence	WQGTIIFPWT	244
CAN54G2	H, Variable region	Murine sequence	cagggtcagttgcagcagctctggaactgagctggtaaggcctgggacitc agtgaagataacctgcaaggctcttgatacagactcactaactttggcta gggtggataaagcagaggcctggacatggacttgaatggattggagatat ttacctggaggtgataatacttactacaatgagaagttcaaggcgaagt cacgtgactgcagacaaatctcgaacacagccatatagcagtcagta gectgacatctgaggactctgtgtctatttctgtttatgattctatactttg gactactgggtcaaggaaacctcagtcaccgtctctcag	245
CAN54G2	II, variable region	Murine sequence	QVQLQQSGTELVRPGTSVKISCKASGYDFTNF WLGWIKRPGHGLEWIGDIYPGGDNTYYNEK FKGKVTLTADKSSNTAYMQFSSLTSEDSAVYF	246

			CFMILYTLDYWGQGSVTVSS	
CAN54G2	II, CDR1	Murine sequence	ggatacgaacttcactaacttugg	247
CAN54G2	II, CDR2	Murine sequence	atttaacctggaggigataatact	248
CAN54G2	II, CDR3	Murine sequence	tttatgattctctatactttggactac	249
CAN54G2	II, CDR1	Murine sequence	GYDFTNFW	250
CAN54G2	II, CDR2	Murine sequence	IYPGGDNT	251
CAN54G2	II, CDR3	Murine sequence	FMILYTLDY	252
CAN30G2	K, Variable region	Murine sequence	gatgttttgatgacccaaactccactctccctgccgtgcagtcctggagatc aagccctccatctctgcagatctagtcagagcattgtacatagtaattggaga cacctattagaaraggtagctgcagaaaccaggccagtcctccaaagctcct gatctacaaagttccaaccgattttctgggtcccagacaggttcagtggtg cagtgatcaggggacagtttcacactcaggatcagcagagtgaggcct gaggatctggggagtttallactgcttcaagggtcacatttccgtggacgtt cgggtggaggccaccaagctggaaatcaaac	253
CAN30G2	K, variable region	Murine sequence	DVLMTQTPLSLPVS LGDQASISCRSSQSIVHSN GDTYLEWY LQKPGQSPKLLIYKVS NRFSGVDP RFSGSGSGTDFTLRISRVEAEDLGVVYCFQGSII FPWTFGGGTKLEIK	254
CAN30G2	K, CDR1	Murine sequence	cagagcattgtacatagtaattggagacacctat	255
CAN30G2	K, CDR2	Murine sequence	aaagttcc	256
CAN30G2	K, CDR3	Murine sequence	ttcaagggtcacatttccgtggacg	257
CAN30G2	K, CDR1	Murine sequence	QSIVHSNGDTY	258
CAN30G2	K, CDR2	Murine sequence	KVS	259
CAN30G2	K, CDR3	Murine sequence	FQGSIIFPWT	260
CAN30G2	II, Variable region	Murine sequence	gatgtgcagctgggtggagtcggggggaggcttagtcagccctggagggt cccggaaactctctgtacagcctctggattcactttcagtagctttggaat gcactgggttcgtcaggctccagagaaggggctggagtgggtcgcatac attagtagtggcagtaglaaaatctactatgcagacacgggtgaaaggccg attcaccatctccagagacaatcccaagaacaccctgttccctgcaaatgac cagtcataaggctcagggacacggccatgtattactgtcuaaggggtggt acgagggggcctgggttgcctactggggccaagggaactctggcactgtc tctgcag	261
CAN30G2	II, variable region	Murine sequence	DVQLVESGGGLVQPGGSRKLSCTASGFTFSSFG MIIWVRQAPKGLEWVAYISSGSSKIYYADTV KGRFTISRDNPKNITLFLQMTSLRSED TAMYYC ARGWYEGAWFAYWGQGLTVTSA	262
CAN30G2	II, CDR1	Murine sequence	ggartcactttcagtagctttgga	263
CAN30G2	II, CDR2	Murine sequence	attagtagtggcagtagtaaaatc	264
CAN30G2	II, CDR3	Murine sequence	gcaagaggggtggtagcagggggcctgggttgcctac	265
CAN30G2	II, CDR1	Murine sequence	GFTFSSFG	266
CAN30G2	II, CDR2	Murine sequence	ISSGSSKI	267
CAN30G2	II, CDR3	Murine sequence	ARGWYEGAWFAY	268

		sequence	
CAN40G1	K, Variable region	Murine sequence gacattgctgacccaatctccagcttcttggctgtctctagggcaga gggcccctccatccctgcaaggccagccaaagtgtgatcatgatggat agltatagaaactggiaaccaacagaaccaggacagccaccaaacct catctatgctacatccaatctagaatctgggateccagccaggttagtgge agtgggtctgggacagacttcacctcaacatccatccigtggaggaggga ggatgctgcaacctattactgtcagcagagttatgaggttccgctcacgttc ggtctctgggaccaagctggagctgaac	269
CAN40G1	K, variable region	Murine sequence DIVLTQSPASLAVSLGQRASISCKASQSVDIIDG DSYMNWYQQKPGQPPKLLIYATSNLESGIPAR FSGSGSGTDFTLNIIIPVEEEDAATYYCQSYEV PLTFGAGTKLELK	270
CAN40G1	K, CDR1	Murine sequence caaaagtgtgatacatgatgggtgatagtat	271
CAN40G1	K, CDR2	Murine sequence gctacatcc	272
CAN40G1	K, CDR3	Murine sequence cagcagagttatgaggttccgctcaog	273
CAN40G1	K, CDR1	Murine sequence QSVDIIDGDSY	274
CAN40G1	K, CDR2	Murine sequence ATS	275
CAN40G1	K, CDR3	Murine sequence QQSYEVPLT	276
CAN40G1	H, Variable region	Murine sequence gaggtccagctgcaacagctctggacctgagctgggaagccctgggctt cagtgaaagataccctgcaggacttctggatacacattcactgaatacaca ttactgggtgagcagagccgtggaaagagccctgagtggttggagg tattaatcctaaacctggtgggtactctctacaaccagaaagttcaaggicaag gccacattgactgtagacaaagctccagcagacgtacatgaggtccg cagcctgacatctgaggatctgcagictattactgtgcaagatttactacg actactggggccaagccacactctcagactctcctcag	277
CAN40G1	H, variable region	Murine sequence EVQLQQSGPELVKPGASVKISCRISGYTFTEYT IHVVKQSRGKSLEWIGGINPNHGGTLYNQKFK VKATLTVDKSSSTAYMELRSLTSEDSAVYYCA RFTYDYWGQGTTTLTVSS	278
CAN40G1	II, CDR1	Murine sequence ggatacacattcactgaatacacc	279
CAN40G1	II, CDR2	Murine sequence altaatcctaaccatgggtgact	280
CAN40G1	II, CDR3	Murine sequence gcaagatttactacgactac	281
CAN40G1	H, CDR1	Murine sequence GYTFTEYT	282
CAN40G1	H, CDR2	Murine sequence INPNHGGT	283
CAN40G1	II, CDR3	Murine sequence ARFTYDY	284
CAN30G1	K, Variable region	Murine sequence gaaaatgtctcaccagctctccagcaatcatgtctgcatctccaggggaa aaggtcacatgacctgcagtgccagctcaagtgttaactacatgcactg gtaccagcagaagtcagcaccctccccaaactctggatttatgacacat ccaaactggcttctggagtcacaggtctgctcagtgccagtggtctgga aactcttactctcagcatcagcagcatggaggtgaagatgttgcactt attactgttttcaggggagtggtgacccgtacacgttcggaggggggacc aagctggaaataaaac	285
CAN30G1	K, variable region	Murine sequence ENVLTQSPAISASPGKVTMTCSASSSVTYM IIWYQQKSSTSPKLWIYDTSKLASGVPGRFSGS GSGNSYSLTISSMEAEDVATYYCFQSGGYPTF GGGTKLEIK	286
CAN30G1	K, CDR1	Murine sequence gacagctcaagtgttaactac	287

		sequence		
CAN30G1	K, CDR2	Murine sequence	gacacatcc	288
CAN30G1	K, CDR3	Murine sequence	tttcaggggagtggtgacctgacacg	289
CAN30G1	K, CDR1	Murine sequence	ASSSVTY	290
CAN30G1	K, CDR2	Murine sequence	DTS	291
CAN30G1	K, CDR3	Murine sequence	FQGSQYPYT	292
CAN30G1	H, Variable region	Murine sequence	cagatccagttggtgcagctggacctgagctgaagaagcctggagaga cagtcagatccctgcaggctctgggtataccttcacaaactatggaat gaactgggtgaagcaggctccaggaaaggggttlaaagtggatgggctg gataaacacctacactggaaagccaacatagttgatgactcaagggac gggttgcctctcttggaaacctctgccaacactgcctattgcagatcaac aacctcaaaaatgaggacacggctacataattctgtgaaagtggagggtac gacgaggactactggggccaaggcaccctcctcacagctcctcag	293
CAN30G1	H, variable region	Murine sequence	QIQLVQSGPELKKPGETVKISCKASGYTFTNYG MNWVKQAPGKGLKWMGWINTYTGKPTYVD DFKGRFAFSLETSANTAYLQINNLIKNDTATYF CESGGYDEDYWGQGTTLTVSS	294
CAN30G1	H, CDR1	Murine sequence	gggtataccctcacaactatgga	295
CAN30G1	H, CDR2	Murine sequence	ataaacacctacactggaaagcca	296
CAN30G1	H, CDR3	Murine sequence	gaaagtggagggtacgacgaggactac	297
CAN30G1	H, CDR1	Murine sequence	GYTFTNYG	298
CAN30G1	H, CDR2	Murine sequence	INTYTGKP	299
CAN30G1	H, CDR3	Murine sequence	ESGGYDEDY	300
CAN30G3	K, Variable region	Murine sequence	gatgtttgatgacccaaactccactcctcctgctcagctctggagatc aagcctccatctcttcagatctagtcagaacattgacatagtaantgaaa cacctatttagaatggtaacctgcagaaatcaggccagctcctcaagctcct gatclacaaagttccaaccgattttctgggtccagacagggtcagtg cagtgatcagggacagattcacactcaagatcagcagagtgagggt gaggatctgggagtttattactgtctcaagggttcacatttccgtggacgtt cgggtggagggcaccagctggaaatcaaac	301
CAN30G3	K, variable region	Murine sequence	DVLMTQTPLSLPVS LGDQASISCRSSQNIVHSN GNTYLEWYLQKSGQSPKLLIYKVS NRIFSGVPD RFSGSGSGTDFTLKISRVEAEDLGVYYCFQGS HFPWTFGGGTKLEIK	302
CAN30G3	K, CDR1	Murine sequence	cagaacattgtacatagtaatggaaacacctat	303
CAN30G3	K, CDR2	Murine sequence	aaagttcc	304
CAN30G3	K, CDR3	Murine sequence	tttcaagggtcacatttccgtggacg	305
CAN30G3	K, CDR1	Murine sequence	QNIVHSNGNTY	306
CAN30G3	K, CDR2	Murine sequence	KVS	307
CAN30G3	K, CDR3	Murine sequence	FQGSIIFPWT	308
CAN30G3	H, Variable	Murine sequence	cagggtgcagctgaaggagtcaggacctggcctgggtggcgccctcacag agcctgtgccatcacatgcactgtctcagggttctccttaaccgactatgga	309

	region		taacctggatcgccagcctccaggaaaagggtctggagtggctgggagt aatatgggggtggggaagcgcatataatttagttctcaaatccagactg agcatcagcaaggacaactccaagagtcaagttttctaaaaatgaacagt ctgcaaacgatgacacagccatgtactactgtgccaacatcggacutg attacgactgctatggactactgggtcaaggaaatttcagtcaccgctcct cag	
CAN30G3	II, variable region	Murine sequence	QVQLKESGPGLVAPSQSLITCTVSGFSLTDYGI TWIRQPPGKGLEWLGVIWGGGSAYYNLVLS RLSISKDNSKSKQVFLKMNSLQTDDETAMYCAK IIRTLITTAMDYWGQGISVTSS	310
CAN30G3	II, CDR1	Murine sequence	gggttctccttaaccgactatggt	311
CAN30G3	H, CDR2	Murine sequence	atatgggggtgggtggaagcgca	312
CAN30G3	II, CDR3	Murine sequence	gccaacatcggaactttgattacgactgctatggactac	313
CAN30G3	H, CDR1	Murine sequence	GFSLTDYG	314
CAN30G3	II, CDR2	Murine sequence	IWGGGSA	315
CAN30G3	II, CDR3	Murine sequence	AKIIRTLITTAMDY	316
CAN30G4	K, Variable region	Murine sequence	gatgtttgatgacccaaactccactctccctgctgtcagttctggagatc aagcctccatctcttgagatctagtcagaaacattgacatagtgatgaaa cacctattagaatggtaactgcagaaaccaggccagtcctcaaaagctcct gatclacaaatltccaaaccgattttctggggctccagacaggttcagtggc agtggatcagggaacagattcacactcaagatcagcagagtggaggctg aggatctgggagtttattactgcttcaagggttcacatgttctccacggttc ggctctgggaccaagctggagctgaaac	317
CAN30G4	K, variable region	Murine sequence	DVLMTQTPLSLPVS LGDQASISCRSSQNVIISD GNTYLEWYLQKPGQSPKLLIYKFSNRFSGVPD RFSGSGSGTDFTLKISRVEAEDLGVYYCFQGSII VPPTFGAGTKLELK	318
CAN30G4	K, CDR1	Murine sequence	cagaaacattgtacatagtgatggaacacctat	319
CAN30G4	K, CDR2	Murine sequence	aaatttcc	320
CAN30G4	K, CDR3	Murine sequence	ttcaagggtcacatgttctctccacg	321
CAN30G4	K, CDR1	Murine sequence	QNVIIISDGNTY	322
CAN30G4	K, CDR2	Murine sequence	KFS	323
CAN30G4	K, CDR3	Murine sequence	FQGSHPPT	324
CAN30G4	II, Variable region	Murine sequence	gaagtgaagctgggtggagctggggaggctttagtgaagctggagggt ccctgaaactctctgtgcagctctgtgattcatttcagttacatgccatg tcgtgggtcgcagattccggagaagagggtggagtgggtcgaacat tagtaatggtgtagttatctactattcagacagtgtagagggtcgaacca ccatctcagagacaatgccagaacacctgtacctgcaaatgagcagt ctgagggtctgaggacacggccatglaaactgtgcacgacataggaggatc ctatagggtacgactgtgtgcttactggggccaaggagctctggcactgt ctctgcag	325
CAN30G4	H, variable region	Murine sequence	EVKLVESGGGLVKSGGSLKLSCAVSGFTFTSY AMSWVRQIPEKRLWVATISNGGSYIYSDSV KGRFTISRDNAKNTLYLQMSSLRSEDAMYCA ARIHRESYRYDWFA YWGQGLVTLSA	326
CAN30G4	II, CDR1	Murine sequence	ggattcatttcagttacatgcc	327

CAN30G4	H, CDR2	Murine sequence	attagtaatgggtgtagttatc	328
CAN30G4	II, CDR3	Murine sequence	gcacgacatagggagtcctataggtacgaactggtttgcctac	329
CAN30G4	H, CDR1	Murine sequence	GFTFSTYA	330
CAN30G4	H, CDR2	Murine sequence	ISNGGSYI	331
CAN30G4	II, CDR3	Murine sequence	ARIRESYRYDWFAY	332
huCAN30G5	K, FR1	Artificial sequence	DIVLTQSPLSLPVTLGQPASISCRSS	333
huCAN30G5	K, FR2	Artificial sequence	LIIWYQQRPGQSPRLIY	334
huCAN30G5	K, FR3	Artificial sequence	NRFSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYC	335
huCAN30G5	K, FR4	Artificial sequence	FGGGTKVEIK	336
huCAN30G5	H, FR1	Artificial sequence	EVQLVESGGGLVQPGGSLKLSCAAS	337
huCAN30G5	H, FR2	Artificial sequence	MHWVRQASGKGLEWVAR	338
huCAN30G5	II, FR3	Artificial sequence	SYAGSVKGRFTVSRDDSKNTFYLMNSLKTEDTAMYYC	339
huCAN30G5	H, FR4	Artificial sequence	WGQGTILVTVSS	340
rehuCAN30G5	K, FR1	Artificial sequence	DIVLTQSPLSLPVTLGQPASISCRSS	341
rehuCAN30G5	K, FR2	Artificial sequence	LHWYLVQKPGQSPRLIY	342
rehuCAN30G5	K, FR3	Artificial sequence	NRFSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYFC	343
rehuCAN30G5	K, FR4	Artificial sequence	FGGGTKLEIK	344
rehuCAN30G5	H, FR1	Artificial sequence	EVQLVESGGGLVQPGGSLKLSCAAS	345
rehuCAN30G5	II, FR2	Artificial sequence	MHWVCQASGKGLEWVAR	346
rehuCAN30G5	II, FR3	Artificial sequence	SYAGSVKGRFTVSRDDSKSLFYLMNNLKTEDTAMYYC	347
rehuCAN30G5	II, FR4	Artificial sequence	WGQGTILVTVSS	348
cdrCAN30G5	K, FR1	Artificial sequence	DVVMTQSPLSLPVTLGQPASISCRSS	349
cdrCAN30G5	K, FR2	Artificial sequence	LNWFQQRPGQSPRLIY	350
cdrCAN30G5	K, FR3	Artificial sequence	NRDSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYC	351
cdrCAN30G5	K, FR4	Artificial sequence	FGGGTKVEIK	352
cdrCAN30G5	II, FR1	Artificial sequence	EVQLVESGGGLVQPGGSLKLSCAAS	353
cdrCAN30G5	H, FR2	Artificial sequence	MHWVRQASGKGLEWVGR	354
cdrCAN30G5	II, FR3	Artificial sequence	AYAASVKGRFTISRDDSKNTAYLMNSLKTEDTAVYYC	355
cdrCAN30G5	II, FR4	Artificial sequence	WGQGTILVTVSS	356

huCAN40G1	K, FR1	Artificial sequence	DIVLTQSPASLAVSLGERATISCKAS	357
huCAN40G1	K, FR2	Artificial sequence	MNWYQQKPGQPPLLIY	358
huCAN40G1	K, FR3	Artificial sequence	NLESGIPARFSGSGSGTDFTLTISLQAEDVATY YC	359
huCAN40G1	K, FR4	Artificial sequence	FGAGTKLEIK	360
huCAN40G1	II, FR1	Artificial sequence	EVQLQQSGPEVKKPGASVKVSCRTS	361
huCAN40G1	II, FR2	Artificial sequence	IIHWVKQAPGKGLEWIGG	362
huCAN40G1	II, FR3	Artificial sequence	LYNQKFKGRVTLTVDKSSSTAYMELSRLRSDD TAVYYC	363
huCAN40G1	II, FR4	Artificial sequence	WGQGTLLTVSS	364
rehuCAN40G1	K, FR1	Artificial sequence	DIVLTQSPASLAVSLGERATISCKAS	365
rehuCAN40G1	K, FR2	Artificial sequence	MNWYQQKPGQPPLLIY	366
rehuCAN40G1	K, FR3	Artificial sequence	NLESGIPARFSGSGSGTDFTLNISVQAEDVAT YYC	367
rehuCAN40G1	K, FR4	Artificial sequence	FGAGTKLELK	368
rehuCAN40G1	H, FR1	Artificial sequence	EVQLQQSGPEVVKPGASVKISCRTS	369
rehuCAN40G1	II, FR2	Artificial sequence	IIHWVKQAPGKGLEWIGG	370
rehuCAN40G1	II, FR3	Artificial sequence	LYNQKFKGRATLTVDKSSSTAYMELSRLRSDD TAVYYC	371
rehuCAN40G1	II, FR4	Artificial sequence	WGQGTLLTVSS	372
cdrCAN40G1	K, FR1	Artificial sequence	DIVMTQSPDSLAVSLGERATINCKSS	373
cdrCAN40G1	K, FR2	Artificial sequence	LAWYQQKPGQPPLLIY	374
cdrCAN40G1	K, FR3	Artificial sequence	TRESGVPDRFSGSGSGTDFTLTISLQAEDVAV YYC	375
cdrCAN40G1	K, FR4	Artificial sequence	FGQGTKEIK	376
cdrCAN40G1	II, FR1	Artificial sequence	QVQLVQSGAEVKKPGASVKVSCCKAS	377
cdrCAN40G1	II, FR2	Artificial sequence	MHWVRQAPGQGLEWMGW	378
cdrCAN40G1	II, FR3	Artificial sequence	NYAQKFQGRVTMTTRDTSISTAYMELSRLRSDD TAVYYC	379
cdrCAN40G1	II, FR4	Artificial sequence	WGQGTLLTVSS	380
huCAN54G2	K, FR1	Artificial sequence	DVVMQTPTLPLPVTLGQPASISCTSS	381
huCAN54G2	K, FR2	Artificial sequence	LNWLLQRPGQSPKRLII	382
huCAN54G2	K, FR3	Artificial sequence	KLDGVPDRFSGSGSGTDFTLKISRVEAEDVGV YYC	383
huCAN54G2	K, FR4	Artificial sequence	FGGGTKVEIK	384
huCAN54G2	II, FR1	Artificial sequence	QVQLQQSGTEVKKPGASVKVSCCKAS	385

huCAN54G2	H, FR2	Artificial sequence	LGWIRQAPGQGLEWIGD	386
huCAN54G2	II, FR3	Artificial sequence	YYNEKFKGRVTLTADKSSNTAYMELSSLRSED TAVYFC	387
huCAN54G2	H, FR4	Artificial sequence	WGQGTLLTVSS	388
rehuCAN54G2	K, FR1	Artificial sequence	DVVMQTQPLTLPTLGQPASISCTSS	389
rehuCAN54G2	K, FR2	Artificial sequence	LNWLLQRPQGSPKRLII	390
rehuCAN54G2	K, FR3	Artificial sequence	KLDSGVPDRISGSGSGTDFTLKISRVEAEDLGIY YC	391
rehuCAN54G2	K, FR4	Artificial sequence	FGGGTKVEIK	392
rehuCAN54G2	II, FR1	Artificial sequence	QVQLQQSGTEVVKPGASVKISCKAS	393
rehuCAN54G2	II, FR2	Artificial sequence	LGWIKQAPGQGLEWIGD	394
rehuCAN54G2	II, FR3	Artificial sequence	YYNEKFKGKVTTLTADKSSNTAYMEFSSLRSED TAVYFC	395
rehuCAN54G2	II, FR4	Artificial sequence	WGQGTLLTVSS	396
cdrCAN54G2	K, FR1	Artificial sequence	DVVMTQSPLSLPVTLGQPASISCRSS	397
cdrCAN54G2	K, FR2	Artificial sequence	LNWFQQRPGQSPRRLIY	398
cdrCAN54G2	K, FR3	Artificial sequence	NRDSGVDPDRFSGSGSGTDFTLKISRVEAEDVGV YYC	399
cdrCAN54G2	K, FR4	Artificial sequence	FGGGTKVEIK	400
cdrCAN54G2	II, FR1	Artificial sequence	QVQLVQSGAEVKKPGASVKVSKAS	401
cdrCAN54G2	II, FR2	Artificial sequence	MHWVRQAPGQGLEWMGI	402
cdrCAN54G2	H, FR3	Artificial sequence	SYAQKFQGRVTMTTRDTSTVYMESSLRSED TAVYYC	403
cdrCAN54G2	II, FR4	Artificial sequence	WGQGTLLTVSS	404

[1057] In one embodiment, an anti-filovirus antibody or antigen-binding portion thereof is a humanized antibody of a murine anti-filovirus antibody. The humanized anti-filovirus antibody or antigen-binding fragment thereof can comprise one or more CDRs of a murine anti-filovirus antibody and one or more human FRs. In one embodiment, the humanized anti-filovirus antibody or antigen-binding fragment thereof comprises one or more CDRs of the murine anti-filovirus antibody CAN30G5, CAN54G2, CAN30G2, CAN40G1, CAN30G1, CAN30G3, or CAN30G4. In one embodiment, the humanized anti-filovirus antibody or antigen-binding fragment thereof comprises one or more human FRs from Table 2.

[1058] In one embodiment, a humanized anti-filovirus antibody or antigen-binding portion thereof comprises a light chain CDR1 comprising an amino acid sequence comprising a sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%,

94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence of SEQ ID NO: 6, 30, 54, 78, 102, 126, 150, 174 or 198; a light chain CDR2 comprising an amino acid sequence comprising a sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence of SEQ ID NO: 7, 31, 55, 79, 103, 127, 151, 175, or 199; a light chain CDR3 comprising an amino acid sequence comprising a sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence of SEQ ID NO: 8, 32, 56, 80, 104, 128, 152, 176, or 200; a heavy chain CDR1 comprising an amino acid sequence comprising a sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence of SEQ ID NO: 18, 42, 66, 90, 114, 138, 162, 186, or 210; a heavy chain CDR2 comprising an amino acid sequence comprising a sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence of SEQ ID NO: 19, 43, 67, 91, 115, 139, 163, 187, or 211; and/or a heavy chain CDR3 comprising an amino acid sequence comprising a sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence of SEQ ID NO: 20, 44, 68, 92, 116, 140, 164, 188, or 212.

[1059] In one embodiment, a humanized anti-filovirus antibody or antigen-binding portion thereof further comprises a light chain FR1 comprising an amino acid sequence comprising a sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence of SEQ ID NO: 333, 341, 349, 357, 365, 373, 381, 389, or 397; a light chain FR2 comprising an amino acid sequence comprising a sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence of SEQ ID NO: 334, 342, 350, 358, 366, 374, 382, 390 or 398; a light chain FR3 comprising an amino acid sequence comprising a sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence of SEQ ID NO: 335, 343, 351, 359, 367, 375, 383, 391 or 399; a light chain FR4 comprising an amino acid sequence comprising a sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence of SEQ ID NO: 336, 344, 352, 360, 368, 376, 384, 392, or

400; a heavy chain FR1 comprising an amino acid sequence comprising a sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence of SEQ ID NOs: 337, 345, 353, 361, 369, 377, 385, 393, or 401; a heavy chain FR2 comprising an amino acid sequence comprising a sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence of SEQ ID NO: 338, 346, 354, 362, 370, 378, 386, 394, or 402; a heavy chain FR3 comprising an amino acid sequence comprising a sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence of SEQ ID NO: 339, 347, 355, 363, 371, 379, 387, 395 or 403; and/or a heavy chain FR4 comprising an amino acid sequence comprising a sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence of SEQ ID NO: 340, 348, 356, 364, 372, 380, 388, 396, or 404.

[1060] In some embodiments, a humanized anti-filovirus antibody or antigen-binding portion thereof comprises: a light chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence comprising SEQ ID NOs: 6, 7 and 8, respectively; a heavy chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence comprising SEQ ID NOs: 18, 19 and 20, respectively; a light chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence comprising SEQ ID NOs: 333, 334, 335 and 336, respectively; and a heavy chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence comprising SEQ ID NOs: 337, 338, 339, and 340, respectively.

[1061] In another embodiment, a humanized anti-filovirus antibody comprises a light chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence comprising SEQ ID NOs: 30, 31, and 32, respectively; a heavy chain CDR1, CDR2, and CDR3 comprising an amino acid sequence

that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence comprising SEQ ID NOs: 42, 43, and 44, respectively; a light chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence e comprising SEQ ID NOs: 341, 342, 343, and 344, respectively; and a heavy chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence comprising SEQ ID NOs: 345, 346, 347, and 348, respectively.

[1062] In another embodiment, a humanized anti-filovirus antibody comprises a light chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence comprising SEQ ID NOs: 54, 55, and 56, respectively; a heavy chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence comprising SEQ ID NOs: 66, 67, and 68, respectively; a light chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence comprising SEQ ID NOs: 349, 350, 351, and 352, respectively; and a heavy chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence comprising SEQ ID NOs: 353, 354, 355, and 356, respectively.

[1063] In another embodiment, a humanized anti-filovirus antibody comprises a light chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence comprising SEQ ID NOs: 78, 79 and 80, respectively; a heavy chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence comprising SEQ ID NOs: 90, 91 and 92, respectively; a light chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%,

92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence comprising SEQ ID NOs: 357, 358, 359 and 360, respectively; and a heavy chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence comprising SEQ ID NOs: 361, 362, 363, and 364, respectively.

[1064] In another embodiment, a humanized anti-filovirus antibody comprises a light chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence comprising SEQ ID NOs: 102, 103, and 104, respectively; a heavy chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence comprising SEQ ID NOs: 114, 115, and 116, respectively; a light chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence comprising SEQ ID NOs: 365, 366, 367, and 368, respectively; and a heavy chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence comprising SEQ ID NOs: 369, 370, 371, and 372, respectively.

[1065] In another embodiment, a humanized anti-filovirus antibody comprises a light chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence comprising SEQ ID NOs: 126, 127, and 128, respectively; a heavy chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence comprising SEQ ID NOs: 138, 139, and 140, respectively; a light chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence comprising SEQ ID NOs: 373, 374, 375, and 376, respectively; and a heavy chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%,

99%, or 100% sequence identity to an amino acid sequence comprising SEQ ID NOs: 377, 378, 379, and 380, respectively;

[1066] In another embodiment, the humanized anti-filovirus antibody comprises a light chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence comprising SEQ ID NOs: 150, 151, and 152, respectively; a heavy chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence comprising SEQ ID NOs: 162, 163, and 164, respectively; a light chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence comprising SEQ ID NOs: 381, 382, 383, and 384, respectively; and a heavy chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence comprising SEQ ID NOs: 385, 386, 387 and 388, respectively.

[1067] In another embodiment, a humanized anti-filovirus antibody comprises a light chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence comprising SEQ ID NOs: 174, 175, and 176, respectively; a heavy chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence comprising SEQ ID NOs: 186, 187, and 188, respectively; a light chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence comprising SEQ ID NOs: 389, 390, 391, and 392, respectively; and a heavy chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence comprising SEQ ID NOs: 393, 394, 395, and 396, respectively.

[1068] In another embodiment, a humanized anti-filovirus antibody comprises a light chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about

85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence comprising SEQ ID NOs: 198, 199 and 200, respectively; a heavy chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence comprising SEQ ID NOs: 210, 211, and 212, respectively; a light chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence comprising SEQ ID NOs: 397, 398, 399, and 400, respectively; and a heavy chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence comprising SEQ ID NOs: 401, 402, 403 and 404, respectively.

[1069] In another embodiment, a humanized anti-filovirus antibody or antigen-binding portion thereof comprises a VH comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to SEQ ID NO: 14, 38, 62, 86, 110, 134, 158, 182, or 206; and/or a VL comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to SEQ ID NO: 2, 26, 50, 74, 98, 122, 146, 170 or 194.

[1070] A humanized anti-filovirus antibody or antigen-binding portion thereof can comprise a VH comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to SEQ ID NO: 14 and a VL comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to SEQ ID NO: 2.

[1071] In some embodiments, a humanized anti-filovirus antibody or antigen-binding portion thereof comprises a VH comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to SEQ ID NO: 38 and a VL comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to SEQ ID NO: 26.

[1072] In some embodiments, a humanized anti-filovirus antibody or antigen-binding portion thereof comprises a VH comprising an amino acid sequence that has at least about

85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to SEQ ID NO: 62 and a VL comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to SEQ ID NO: 50.

[1073] In some embodiments, a humanized anti-filovirus antibody or antigen-binding portion thereof comprises a VH comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to SEQ ID NO: 86 and a VL comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to SEQ ID NO: 74.

[1074] In some embodiments, a humanized anti-filovirus antibody or antigen-binding portion thereof comprises a VH comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to SEQ ID NO: 110 and a VL comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to SEQ ID NO: 98.

[1075] In some embodiments, a humanized anti-filovirus antibody or antigen-binding portion thereof comprises a VH comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to SEQ ID NO: 134 and a VL comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to SEQ ID NO: 122.

[1076] In some embodiments, a humanized anti-filovirus antibody or antigen-binding portion thereof comprises a VH comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to SEQ ID NO: 158 and a VL comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to SEQ ID NO: 146.

[1077] In some embodiments, a humanized anti-filovirus antibody or antigen-binding portion thereof comprises a VH comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to SEQ ID NO: 182 and a VL comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to SEQ ID NO: 170.

[1078] In some embodiments, a humanized anti-filovirus antibody or antigen-binding portion thereof comprises a VH comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to SEQ ID NO: 206 and a VL comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to SEQ ID NO: 194.

[1079] In one embodiment, a humanized anti-filovirus antibody or antigen-binding portion thereof comprises a light chain CDR1 comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence encoded by a nucleotide sequence of SEQ ID NO: 3, 27, 51, 75, 99, 123, 147, 171 or 195; a light chain CDR2 comprising an amino acid sequence comprising a sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence encoded by a nucleotide sequence of SEQ ID NO: 4, 28, 52, 76, 100, 124, 148, 172, or 196; a light chain CDR3 comprising an amino acid sequence comprising a sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence encoded by a nucleotide sequence of SEQ ID NO: 5, 29, 53, 77, 101, 125, 149, 173, or 197; a heavy chain CDR1 comprising an amino acid sequence comprising a sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence encoded by a nucleotide sequence of SEQ ID NO: 15, 39, 63, 87, 111, 135, 159, 183, or 207; a heavy chain CDR2 comprising an amino acid sequence comprising a sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence encoded by a nucleotide sequence of SEQ ID NO: 16, 40, 64, 88, 112, 136, 160, 184, or 208; and/or a heavy chain CDR3 comprising an amino acid sequence comprising a sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence encoded by a nucleotide sequence of SEQ ID NO: 17, 41, 65, 89, 113, 137, 161, 185 or 209.

[1080] In one embodiment, a humanized anti-filovirus antibody or antigen-binding portion thereof further comprises a light chain FR1 comprising an amino acid sequence comprising a sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid

sequence encoded by a nucleotide sequence of SEQ ID NO: 9, 33, 57, 81, 105, 129, 153, 177, or 201; a light chain FR2 comprising an amino acid sequence comprising a sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence encoded by a nucleotide sequence of SEQ ID NO: 10, 34, 58, 82, 106, 130, 154, 178, or 202; a light chain FR3 comprising an amino acid sequence comprising a sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence encoded by a nucleotide sequence of SEQ ID NO: 11, 35, 59, 83, 107, 131, 155, 179 or 203; a light chain FR4 comprising an amino acid sequence comprising a sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence encoded by a nucleotide sequence of SEQ ID NO: 12, 36, 60, 84, 108, 132, 156, 180 or 204; a heavy chain FR1 comprising an amino acid sequence comprising a sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence encoded by a nucleotide sequence of SEQ ID NOs: 21, 45, 69, 93, 117, 141, 165, 189, or 213; a heavy chain FR2 comprising an amino acid sequence comprising a sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence encoded by a nucleotide sequence of SEQ ID NO: 22, 46, 70, 94, 118, 142, 166, 190 or 214; a heavy chain FR3 comprising an amino acid sequence comprising a sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence encoded by a nucleotide sequence of SEQ ID NO: 23, 47, 71, 95, 119, 143, 167, 191 or 215; and/or a heavy chain FR4 comprising an amino acid sequence comprising a sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence encoded by a nucleotide sequence of SEQ ID NO: 24, 48, 72, 96, 120, 144, 168, 192 or 216.

[1081] In some embodiments, a humanized anti-filovirus antibody or antigen-binding portion thereof comprises: a light chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence encoded by a nucleotide sequence of SEQ ID NOs: 3, 4, and 5, respectively; a heavy chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85%,

86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence encoded by a nucleotide sequence of SEQ ID NOs: 15, 16, and 17, respectively; a light chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence encoded by a nucleotide sequence of SEQ ID NOs: 9, 10, 11, and 12, respectively; and a heavy chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence encoded by a nucleotide sequence of SEQ ID NOs: 21, 22, 23, and 24, respectively.

[1082] In another embodiment, a humanized anti-filovirus antibody comprises a light chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence encoded by a nucleotide sequence of SEQ ID NOs: 27, 28, and 29, respectively; a heavy chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence encoded by a nucleotide sequence of SEQ ID NOs: 39, 40, and 41, respectively; a light chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence encoded by a nucleotide sequence of SEQ ID NOs: 33, 34, 35, and 36, respectively; and a heavy chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence encoded by a nucleotide sequence of SEQ ID NOs: 45, 46, 47 and 48, respectively.

[1083] In another embodiment, a humanized anti-filovirus antibody comprises a light chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence encoded by a nucleotide sequence of SEQ ID NOs: 51, 52, and 53, respectively; a heavy chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence encoded by a nucleotide sequence of SEQ ID NOs: 63, 64, and 65,

respectively; a light chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence encoded by a nucleotide sequence of SEQ ID NOs: 57, 58, 59 and 60, respectively; and a heavy chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence encoded by a nucleotide sequence of SEQ ID NOs: 69, 70, 71, and 72, respectively.

[1084] In another embodiment, a humanized anti-filovirus antibody comprises a light chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence encoded by a nucleotide sequence of SEQ ID NOs: 75, 76, and 77, respectively; a heavy chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence encoded by a nucleotide sequence of SEQ ID NOs: 87, 88, and 89, respectively; a light chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence encoded by a nucleotide sequence of SEQ ID NOs: 81, 82, 83, and 84, respectively; and a heavy chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence encoded by a nucleotide sequence of SEQ ID NOs: 93, 94, 95, and 96, respectively.

[1085] In another embodiment, a humanized anti-filovirus antibody comprises a light chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence encoded by a nucleotide sequence of SEQ ID NOs: 99, 100, and 101, respectively; a heavy chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence encoded by a nucleotide sequence of SEQ ID NOs: 111, 112, and 113, respectively; a light chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%,

97%, 98%, 99%, or 100% sequence identity to an amino acid sequence encoded by a nucleotide sequence of SEQ ID NOs: 105, 106, 107, and 108, respectively; and a heavy chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence encoded by a nucleotide sequence of SEQ ID NOs: 117, 118, 119, and 120, respectively.

[1086] In another embodiment, a humanized anti-filovirus antibody comprises a light chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence encoded by a nucleotide sequence of SEQ ID NOs: 123, 124 and 125, respectively; a heavy chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence encoded by a nucleotide sequence of SEQ ID NOs: 135, 136, and 137, respectively; a light chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence encoded by a nucleotide sequence of SEQ ID NOs: 129, 130, 131, and 132, respectively; and a heavy chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence encoded by a nucleotide sequence of SEQ ID NOs: 141, 142, 143, and 144, respectively.

[1087] In another embodiment, the humanized anti-filovirus antibody comprises a light chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence encoded by a nucleotide sequence of SEQ ID NOs: 147, 148 and 149, respectively; a heavy chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence encoded by a nucleotide sequence of SEQ ID NOs: 159, 160, and 161, respectively; a light chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence encoded by a nucleotide sequence of SEQ ID NOs: 153, 154, 155, and 156, respectively; and a heavy chain

FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence encoded by a nucleotide sequence of SEQ ID NOs: 165, 166, 167, and 168, respectively.

[1088] In another embodiment, a humanized anti-filovirus antibody comprises a light chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence encoded by a nucleotide sequence of SEQ ID NOs: 171, 172, and 173, respectively; a heavy chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence encoded by a nucleotide sequence of SEQ ID NOs: 183, 184, and 185, respectively; a light chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence encoded by a nucleotide sequence of SEQ ID NOs: 177, 178, 179 and 180, respectively; and a heavy chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence encoded by a nucleotide sequence of SEQ ID NOs: 189, 190, 191, and 192, respectively.

[1089] In another embodiment, a humanized anti-filovirus antibody comprises a light chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence encoded by a nucleotide sequence of SEQ ID NOs: 195, 196 and 197, respectively; a heavy chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence encoded by a nucleotide sequence of SEQ ID NOs: 207, 208, and 209, respectively; a light chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence encoded by a nucleotide sequence of SEQ ID NOs: 201, 202, 203 and 204, respectively; and a heavy chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or

100% sequence identity to an amino acid sequence encoded by a nucleotide sequence of SEQ ID NOs: 213, 214, 215 and 216, respectively.

[1090] In another embodiment, a humanized anti-filovirus antibody or antigen-binding portion thereof comprises a VH comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence encoded by a nucleotide sequence of SEQ ID NO: 13, 37, 61, 85, 109, 133, 157, 181, or 205; and/or a VL comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence encoded by a nucleotide sequence of SEQ ID NO: 1, 25, 49, 73, 97, 121, 145, 169, or 193.

[1091] A humanized anti-filovirus antibody or antigen-binding portion thereof can comprise a VH comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence encoded by a nucleotide sequence of SEQ ID NO: 13 and a VL comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence encoded by a nucleotide sequence of SEQ ID NO: 1.

[1092] In some embodiments, a humanized anti-filovirus antibody or antigen-binding portion thereof comprises a VH comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence encoded by a nucleotide sequence of SEQ ID NO: 37 and a VL comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence encoded by a nucleotide sequence of SEQ ID NO: 25.

[1093] In some embodiments, a humanized anti-filovirus antibody or antigen-binding portion thereof comprises a VH comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence encoded by a nucleotide sequence of SEQ ID NO: 61 and a VL comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or

100% sequence identity to an amino acid sequence encoded by a nucleotide sequence of SEQ ID NO: 49.

[1094] In some embodiments, a humanized anti-filovirus antibody or antigen-binding portion thereof comprises a VH comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence encoded by a nucleotide sequence of SEQ ID NO: 85 and a VL comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence encoded by a nucleotide sequence of SEQ ID NO: 73.

[1095] In some embodiments, a humanized anti-filovirus antibody or antigen-binding portion thereof comprises a VH comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence encoded by a nucleotide sequence of SEQ ID NO: 109 and a VL comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence encoded by a nucleotide sequence of SEQ ID NO: 97.

[1096] In some embodiments, a humanized anti-filovirus antibody or antigen-binding portion thereof comprises a VH comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence encoded by a nucleotide sequence of SEQ ID NO: 133 and a VL comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence encoded by a nucleotide sequence of SEQ ID NO: 121.

[1097] In some embodiments, a humanized anti-filovirus antibody or antigen-binding portion thereof comprises a VH comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence encoded by a nucleotide sequence of SEQ ID NO: 157 and a VL comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence encoded by a nucleotide sequence of SEQ ID NO: 145.

[1098] In some embodiments, a humanized anti-filovirus antibody or antigen-binding portion thereof comprises a VH comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence encoded by a nucleotide sequence of SEQ ID NO: 181 and a VL comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence encoded by a nucleotide sequence of SEQ ID NO: 169.

[1099] In some embodiments, a humanized anti-filovirus antibody or antigen-binding portion thereof comprises a VH comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence encoded by a nucleotide sequence of SEQ ID NO: 205 and a VL comprising an amino acid sequence that has at least about 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to an amino acid sequence encoded by a nucleotide sequence of SEQ ID NO: 193.

[1100] Another aspect of the present disclosure is a multispecific molecule comprising a humanized anti-filovirus antibody or antigen-binding portion thereof disclosed herein. A multispecific molecule has specificity for at least two different antigens or epitopes. While such a molecule generally binds to two antigens (*i.e.*, bispecific molecule or antibody), the term "multispecific molecule" in the present invention encompasses an anti-filovirus antibody having specificity for two or more (such as three) antigens. A multispecific molecule comprising an anti-filovirus antibody or antigen-binding portion thereof binds at least one epitope of a filovirus. In some embodiments, the two or more antigens are filovirus antigens. In some embodiments, the two or more antigens include an antigen that is not a filovirus antigen.

[1101] A multispecific molecule may comprise a full length antibody or a fragment of such an antibody. In one embodiment, the anti-filovirus antibody is a scFv dimer or diabody rather than whole antibody. Diabodies and scFv can be constructed without an Fc region, using only variable domains. Diabodies are bivalent, bispecific antibodies in which V_H and V_L domains are expressed on a single polypeptide chain, but using a linker that is too short to allow for pairing between the two domains on the same chain, thereby forcing the domains to pair with complementary domains of another chain and creating two antigen binding sites.

[1102] In one embodiment, the multivalent or multispecific anti-filovirus antibody comprises two dimerized single chain polypeptides. For instance, in one embodiment, each single chain polypeptide comprises, from amino to carboxyl terminus, a first binding domain (*e.g.*, scFv), an immunoglobulin hinge region, an immunoglobulin constant region (with or without a CHI region), a c-terminus linker, and a second binding domain. The c-terminus linker may comprise, for instance, an amino acid linker derived from an amino acid sequence of an immunoglobulin hinge region (*e.g.*, an immunoglobulin “core” hinge region) or an amino acid sequence derived from a stalk region of a type II C lectin (*e.g.*, NKG2A, NKG2D). In one embodiment, the c-terminus linker comprises an amino acid sequence such as (A₄S)³ or (G₄S)³. The single chain polypeptide may also comprise a heterodimerization domain so that each single chain polypeptide dimerizes with a different single chain polypeptide such that a heterodimer is formed with up to four different binding domains.

[1103] The disclosure also includes nucleic acids (*e.g.*, DNA or RNA) encoding an anti-filovirus antibody or antigen-binding portion thereof described herein. Nucleic acids of the disclosure include nucleic acids comprising a region that is substantially identical to a polynucleotide as listed in Table 2. Nucleic acids of the disclosure also include complementary nucleic acids. The nucleic acid sequences provided herein can be exploited using codon optimization, degenerate sequence, silent mutations, and other DNA techniques to optimize expression in a particular host, and the present disclosure encompasses such sequence modifications.

[1104] Nucleic acids encoding an anti-filovirus antibody or antigen-binding portion thereof described herein can be propagated by placing the nucleic acids in a vector. The choice of appropriate vector is well within the skill of the art. Many such vectors are available commercially. A nucleic acid encoding an antibody or antigen-binding portion thereof disclosed herein, a nucleic acid molecule encoding the polypeptide, operably linked to regulatory sequences that control transcriptional expression in an expression vector, is introduced into a host cell. In addition to transcriptional regulatory sequences, such as promoters and enhancers, expression vectors can include translational regulatory sequences and a marker gene which is suitable for selection of cells that carry the expression vector. The gene product encoded by a polynucleotide of the disclosure is expressed in any convenient expression system, including, for example, bacterial, yeast, insect, amphibian and mammalian systems.

[1105] The disclosure includes an expression vector comprising a nucleic acid segment, wherein the nucleic acid segment may comprise a nucleotide sequence with the following

sequences: (a) SEQ ID NOs: 3, 4, 5, 9, 10, 11, 12, 15, 16, 17, 21, 22, 23, and 24; (b) SEQ ID NOs: 27, 28, 29, 33, 34, 35, 36, 39, 40, 41, 45, 46, 47, and 48; (c) SEQ ID NOs: 51, 52, 53, 57, 58, 59, 60, 63, 64, 65, 69, 70, 71, and 72; (d) SEQ ID NOs: 75, 76, 77, 81, 82, 83, 84, 87, 88, 89, 93, 94, 95, and 96; (e) SEQ ID NOs: 99, 100, 101, 105, 106, 107, 108, 111, 112, 113, 117, 118, 119, and 120; (f) SEQ ID NOs: 123, 124, 125, 129, 130, 131, 132, 135, 136, 137, 141, 142, 143, and 144; (g) SEQ ID NOs: 147, 148, 149, 153, 154, 155, 156, 159, 160, 161, 165, 166, 167, and 168; (h) SEQ ID NOs: 171, 172, 173, 177, 178, 179, 180, 183, 184, 185, 189, 190, 191, and 192; (i) SEQ ID NOs: 195, 196, 197, 201, 202, 203, 204, 207, 208, 209, 213, 214, 215 and 216; a nucleotide sequence that has at least about 70%, 75%, 80%, 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to one of the nucleotide sequences of (a)-(i); or a nucleotide sequence encoding the same amino acids as one of the nucleotide sequences of (a)-(i).

[1106] In some embodiments, an expression vector comprises a nucleotide sequence with the following sequences: (a) SEQ ID NOs: 1 and 13; (b) SEQ ID NOs: 25 and 37; (c) SEQ ID NOs: 49 and 61; (d) SEQ ID NOs: 73 and 85; (e) SEQ ID NOs: 97 and 109; (f) SEQ ID NOs: 121 and 133; (g) SEQ ID NOs: 145 and 157; (h) SEQ ID NOs: 169 and 181; (i) SEQ ID NOs: 193 and 205; a nucleotide sequence that has at least about 70%, 75%, 80%, 85%, 86%, 87%, 88%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to one of the nucleotide sequences of (a)-(i); or a nucleotide sequence encoding the same amino acids as one of the nucleotide sequences of (a)-(i).

[1107] Also provided herein is a host cell comprising an expression vector disclosed herein. Accordingly, antibodies and antigen-binding portions thereof disclosed herein can be produced in genetically engineered host cells according to conventional techniques. Suitable host cells are those cell types that can be transformed or transfected with exogenous DNA and grown in culture, and include bacterial, eukaryotic or mammalian cells, such as cultured higher eukaryotic cells (including cultured cells of multicellular organisms), particularly cultured mammalian cells. Cultured mammalian cells are suitable hosts for production of recombinant proteins for use within the present disclosure. Examples of suitable mammalian host cells include COS-1, COS-7, HEK293, BHK21, CHO, BSC-1, HepG2, SP2/0, HeLa, myeloma or lymphoma cell. Other mammalian host cells include African green monkey kidney cells (Vero; ATCC CRL 1587), human embryonic kidney cells (293-HEK; ATCC CRL 1573), baby hamster kidney cells (BHK-21, BHK-570; ATCC CRL 8544, ATCC CRL 10314), canine kidney cells (MDCK; ATCC CCL 34), Chinese hamster ovary cells (CHO-K1; ATCC CCL61; CHO DG44; CHO DXB11 (Hyclone, Logan, UT); *see also, e.g.*, Chasin

et al., *Som. Cell. Molec. Genet.* 12:555, 1986)), rat pituitary cells (GH1; ATCC CCL82), HeLa S3 cells (ATCC CCL2.2), rat hepatoma cells (H-4-II-E; ATCC CRL 1548) SV40-transformed monkey kidney cells (COS-1; ATCC CRL 1650) and murine embryonic cells (NIH-3T3; ATCC CRL 1658). Additional suitable cell lines are known in the art and available from public depositories such as the American Type Culture Collection, Manassas, Virginia.

[1108] The present disclosure also provides a composition comprising an anti-filovirus antibody or antigen-binding portion thereof and one or more other antibodies or antigen-binding portions thereof, wherein the one or more other antibodies or antigen-binding portions thereof binds a protein produced by a virus in the *Filoviridae* family. The one or more other antibodies or antigen-binding portions thereof can bind a glycoprotein, such as GP (e.g., GP1 or GP2). In some embodiments, the one or more other antibodies or antigen-binding portions thereof binds *Ebolavirus* and/or *Marburgvirus*, such as *Zaire ebolavirus*, *Sudan ebolavirus*, *Reston ebolavirus*, *Tai Forest ebolavirus*, *Bundibugyo ebolavirus*, *Cote d'Ivoire ebolavirus*, *Marburg virus* or *Ravn virus*. In some embodiments, the composition further comprises a pharmaceutically acceptable carrier.

[1109] In some embodiments, a composition comprising an anti-filovirus antibody or antigen-binding portion thereof disclosed herein with another antibody or antigen-binding portion thereof act synergistically when administered to a subject in need. As used herein, "synergy" or a "synergistic" response refers to an activity or improvement (e.g., prevents infection with a filovirus, prevents disease associated with a filovirus infection, reduces the number and/or severity of symptoms of a filovirus infection, stops or limits the spread of a filovirus, and/or shortens the duration of a filovirus infection at a rate) that is greater than the sum of the effect of each therapy as a monotherapy. As can be appreciated by a skilled artisan, synergy can be shown *in vitro*, *ex vivo* and *in vivo*.

[1110] As will be appreciated by one of skill in the art, the antibody or antigen-binding portion thereof may be used in the preparation of a medicament or pharmaceutical composition for administration (either therapeutic or prophylactic) to a subject in need of such treatment. In these embodiments, the medicament or pharmaceutical composition is prepared by mixing the antibody or antigen-binding portion thereof with a pharmaceutically acceptable carrier. The resulting composition is pharmacologically acceptable if its administration can be tolerated by a recipient patient. Accordingly, another aspect of the present disclosure is a pharmaceutical composition comprising an anti-filovirus antibody or antigen-binding portion thereof disclosed herein and a pharmaceutically acceptable carrier.

The pharmaceutical composition can comprise a pharmaceutically acceptable carrier, diluent, excipient, and/or other additives, such as water, a pharmaceutical acceptable organic solvent, collagen, polyvinyl alcohol, polyvinylpyrrolidone, a carboxyvinyl polymer, carboxymethylcellulose sodium, polyacrylic sodium, sodium alginate, water-soluble dextran, carboxymethyl starch sodium, pectin, methyl cellulose, ethyl cellulose, xanthan gum, gum Arabic, casein, gelatin, agar, diglycerin, glycerin, propylene glycol, polyethylene glycol, Vaseline, paraffin, stearyl alcohol, stearic acid, human serum albumin (HSA), mannitol, sorbitol, lactose, a pharmaceutically acceptable surfactant and the like. Additives used are chosen from, but not limited to, the above or combinations thereof, as appropriate, depending on the dosage form of the present invention.

[1111] Formulation of the composition will vary according to the route of administration selected (e.g., solution, emulsion). An appropriate composition comprising the active agent to be administered can be prepared in a physiologically acceptable vehicle or carrier. For solutions or emulsions, suitable carriers include, for example, aqueous or alcoholic/aqueous solutions, emulsions or suspensions, including saline and buffered media. Parenteral vehicles can include sodium chloride solution, Ringer's dextrose, dextrose and sodium chloride, lactated Ringer's or fixed oils. Intravenous vehicles can include various additives, preservatives, or fluid, nutrient or electrolyte replenishers

[1112] The pharmaceutical compositions may be in the form of a sterile injectable aqueous, oleaginous suspension, dispersions or sterile powders for the extemporaneous preparation of sterile injectable solutions or dispersions. The suspension may be formulated according to the known art using those suitable dispersing or wetting agents and suspending agents which have been mentioned above. The sterile injectable preparation may also be a sterile injectable solution or suspension in a non-toxic parenterally-acceptable diluent or solvent, for example as a solution in 1,3-butane diol. The carrier can be a solvent or dispersion medium containing, for example, water, ethanol, polyol (for example, glycerol, propylene glycol, and liquid polyethylene glycol, and the like), suitable mixtures thereof, vegetable oils, Ringer's solution and isotonic sodium chloride solution. In addition, sterile, fixed oils are conventionally employed as a solvent or suspending medium. For this purpose any bland fixed oil may be employed including synthetic mono- or diglycerides. In addition, fatty acids such as oleic acid find use in the preparation of injectables.

[1113] In all cases the form should be sterile and must be fluid to the extent that easy syringability exists. The proper fluidity can be maintained, for example, by the use of a coating, such as lecithin, by the maintenance of the required particle size in the case of

dispersion and by the use of surfactants. It must be stable under the conditions of manufacture and storage and must be preserved against the contaminating action of microorganisms, such as bacteria and fungi. The prevention of the action of microorganisms can be brought about by various antibacterial and antifungal agents, for example, parabens, chlorobutanol, phenol, sorbic acid, thimerosal, and the like. In many cases, it will be desirable to include isotonic agents, for example, sugars or sodium chloride. Prolonged absorption of the injectable compositions can be brought about by the use in the compositions of agents delaying absorption, for example, aluminum monostearate and gelatin.

[1114] Compositions useful for administration may be formulated with uptake or absorption enhancers to increase their efficacy. Such enhancers include for example, salicylate, glycocholate/linoleate, glycholate, aprotinin, bacitracin, SDS, caprate and the like. See, e.g., Fix (*J. Pharm. Sci.*, 85:1282-1285, 1996) and Oliyai and Stella (*Ann. Rev. Pharmacol. Toxicol.*, 32:521-544, 1993).

[1115] In some embodiments, the present disclosure provides methods for reducing, preventing, or treating a filovirus infection in a subject in need thereof. In some embodiments, a subject in need thereof includes a subject that has been infected with a filovirus, is showing symptoms consistent with a filovirus infection, is exhibiting a filovirus infection, is suspected of having a filovirus infection, or is at risk of developing a filovirus infection. Thus, in some embodiments, provided herein is a method of treating a filovirus infection or outbreak comprising administering a therapeutically or prophylactically effective amount of an anti-filovirus antibody or antigen-binding portion thereof to an individual in need of such treatment. In some embodiments, the filovirus infection or outbreak is a *Marburgvirus* infection. In other embodiments, the infection is an *Ebolavirus* infection.

[1116] In one aspect, the antibodies or antigen-binding portion thereof may be formulated into a pharmaceutical product for providing treatment for individuals for filovirus infection, comprising a therapeutically effective amount of said antibody or antigen-binding portion. In some embodiments, an effective amount of the antibody or antigen-binding portion thereof may be formulated into a pharmaceutical product for treating an individual who has been infected with or exposed to a filovirus, who is at risk of a filovirus infection, or who is displaying symptoms of a filovirus infection (e.g., a *Marburgvirus* or *Ebolavirus* infection). A therapeutically effective amount can be determined by the skilled person. The therapeutically effective dosage of the pharmaceutical composition can be determined readily by the skilled artisan, for example, from animal studies. In addition, human clinical studies

can be performed to determine the preferred effective dose for humans by a skilled artisan. The precise dose to be employed will also depend on the route of administration.

[1117] In some embodiments, the antibodies and antigen-binding portions provided herein may be administered via enteral (including without limitation oral administration and rectal administration) or parenteral (including without limitation intravenous administration, intramuscular administration, and aerosol delivery) administration. Additional exemplary appropriate methods for administration of the antibodies and antigen-binding fragments provided herein include nasal, buccal, vaginal, ophthalmic, subcutaneous, intraperitoneal, intraarterial, spinal, intrathecal, intra-articular, intra-arterial, sub-arachnoid, sublingual, oral mucosal, bronchial, lymphatic, intra-uterine, integrated on an implantable device such as a suture or in an implantable device such as an implantable polymer, intradural, intracortical, or dermal. Such compositions would normally be administered as pharmaceutically acceptable compositions as described herein. In some embodiments, the antibodies or antigen-binding portions thereof may be administered to the subject once per day, or in multiple doses per day. In one embodiment, the antibodies or antigen-binding portions thereof are administered to the subject until symptoms improve or resolve and/or until the subject is no longer at risk of a filovirus infection.

[1118] As used herein, the term “subject” or “patient” refers to any member of the subphylum cordata, including, without limitation, humans and other primates, including non-human primates such as chimpanzees and other apes and monkey species. Farm animals such as cattle, sheep, pigs, goats and horses; domestic mammals such as dogs and cats; laboratory animals including rodents such as mice, rats (including cotton rats) and guinea pigs; birds, including domestic, wild and game birds such as chickens, turkeys and other gallinaceous birds, ducks, geese, and the like are also non-limiting examples. The terms “mammals” and “animals” are included in this definition. Both adult and newborn individuals are intended to be covered. In particular, the methods and compositions provided herein are methods and compositions for treating filovirus infections in human subjects.

[1119] In general, it is desirable to provide the recipient with a dosage of antibody which is in the range of from about 1 µg/kg body weight of individual to 1 g/kg body weight. It is of note that many factors are involved in determining what is a therapeutically effective dose or effective amount such as, for example but by no means limited to, the patient’s age, weight, sex and general condition. Effective amounts may also vary according to the quality of the preparation and the severity of the infection or outbreak. Accordingly, it is noted that one of

skill in the art will be able to determine what constitutes an “effective amount” based on a particular set of circumstances without undue experimentation.

[1120] In some embodiments, the antibody or antigen-binding portion thereof is “protective” or “neutralizing” and accordingly on administration will hinder the spread of the virus. In some embodiments, the antibodies and antigen-binding portions thereof provided herein interfere either with viral attachment, entry and/or unpackaging once inside the cell. Accordingly, in some embodiments, administering an effective amount to an individual in need of such treatment will result in at least one of the following: reduced viral load, reduction in severity of symptoms associated with the filovirus infection, and reduced or slowed viral reproduction.

[1121] In other embodiments of the invention, the antibody or antigen-binding portion thereof described herein may be used in a method for detecting a filovirus (e.g., *Marburgvirus* or *Ebolavirus*) in a sample suspected of containing the filovirus. In other embodiments, the antibody or antigen-binding portion thereof described herein may be used in a method for diagnosing a filovirus infection. Such methods are well known in the art and a wide variety of suitable methods will be readily apparent to one of skill in the art. Such methods may involve contacting the sample to be investigated with the antibody or antigen-binding fragment thereof under conditions suitable for binding, and then detecting the bound antibody or fragment. The sample may be, for example, a biological sample, such as cells, tissue, biological fluid or the like or may be an environmental sample such as a soil or water sample or a food sample such as canned goods, meats and the like. Other suitable samples will be readily apparent to one of skill in the art.

[1122] As will be appreciated by one of skill in the art, detection antibodies must show high specificity and avidity for their antigenic target. As such, showing that a monoclonal antibody or antigen-binding fragment thereof reacts with the antigenic target derived from a highly purified or in vitro prepared sample does not guarantee that the antibody has sufficient specificity for use with biological sample. That is, the antibody must have sufficient specificity that it will not produce false positives or react with antigens from related, viruses. Examples of suitable tests for determining utility as a diagnostic or as a neutralizing mAb include but are by no means limited to negative neutralization and/or negative detection of a non-filovirus, or C-ELISA data showing competition of binding with the mouse mAbs that is being detected thereby showing that the mAbs can be used to show that an immune response to filovirus has occurred in patient/animal sera, meaning that they were exposed/infected (abrogation of binding by human antibodies). Alternatively, biological material such as

blood, mucus or stool with could be spiked or enriched with the virus and the monoclonal antibodies used to detect added virus in the sample, which would in turn determine limits of detection as well as other parameters of the monoclonal antibodies. Biological samples from experimentally infected animals could also be used to determine the utility of the mAbs at different stages of the infection cycle.

[1123] In some embodiments, at least one of the detection antibodies is mixed with a biological sample under suitable conditions to promote binding of the at least one detection antibody with the antigenic target if the antigenic target is present in the biological sample. Binding of the detection antibody to an antigenic target within the sample is then detected using means known in the art, for example, by use of a labelled secondary antibody or other means discussed herein and/or known in the art. In some embodiments, the detection antibody (e.g., an anti-filovirus antibody disclosed herein) is labelled.

[1124] While various embodiments have been described above, it should be understood that they have been presented by way of example, and not limitation. Where methods described above indicate certain events occurring in certain order, the ordering of certain events can be modified. Additionally, certain of the events may be performed concurrently in a parallel process when possible, as well as performed sequentially as described above.

[1125] All publications, patents and patent applications discussed and cited herein are incorporated herein by reference in their entireties. It is understood that the disclosed invention is not limited to the particular methodology, protocols and materials described as these can vary. It is also understood that the terminology used herein is for the purposes of describing particular embodiments only and is not intended to limit the scope of the present invention which will be limited only by the appended claims.

EXAMPLES

[1126] The invention will be further clarified by the following examples, which are intended to be purely exemplary of the invention and in no way limiting.

Example 1: V Gene Sequencing

[1127] V gene sequencing for CAN30G5 was performed by first isolating RNA from the CAN30G5 parental hybridoma clonal cell line using the RNAeasy Mini Kit. A panel of specific primers for each variable gene group was used to amplify the cDNA in a single step RT-PCR reaction to generate cDNA encoding the heavy and light chain variable domains

(VH and VL) of CAN30G5. The cDNAs were cloned and sequenced using standard techniques. After sequencing and identification of the variable gene, subgroup specific leader primers were designed to remove potential mutations from degenerate primers in the original primer panel to ensure sequence identity of the full variable gene sequence. The cDNA sequences encoding the VL and VH of CAN30G5 are presented as SEQ ID NO: 221 and SEQ ID NO: 229, respectively, and the amino acid sequences are shown as SEQ ID NO: 222 and SEQ ID NO: 230, respectively. The amino acid sequences of the three light chain complementarity determining regions LCDR1, LCDR2, and LCDR3 are presented as SEQ ID NO: 226, SEQ ID NO: 227, and SEQ ID NO: 228, respectively, and the HCDR1, HCDR2, and HCDR3 regions are presented as SEQ ID NO: 234, SEQ ID NO: 235, and SEQ ID NO: 236, respectively.

[1128] V gene sequencing for the CAN40G1 parental hybridoma clonal cell line follows the same procedure as described above for CAN30G5. The cDNA sequences encoding the VL and VH of CAN40G1 are presented as SEQ ID NO: 269 and SEQ ID NO: 277, respectively, and the amino acid sequences are shown as SEQ ID NO: 270 and SEQ ID NO: 278, respectively. The amino acid sequences of the three light chain complementarity determining regions LCDR1, LCDR2, and LCDR3 are presented as SEQ ID NO: 274, SEQ ID NO: 275, and SEQ ID NO: 276, respectively, and the HCDR1, HCDR2, and HCDR3 regions are presented as SEQ ID NO: 282, SEQ ID NO: 283, and SEQ ID NO: 284, respectively.

[1129] V gene sequencing for the CAN54G2 parental hybridoma clonal cell line follows the same procedure as described above for CAN30G5. The cDNA sequences encoding the VL and VH of CAN54G2 are presented as SEQ ID NO: 237 and SEQ ID NO: 245, respectively, and the amino acid sequences are shown as SEQ ID NO: 238 and SEQ ID NO: 246, respectively. The amino acid sequences of the three light chain complementarity determining regions LCDR1, LCDR2, and LCDR3 are presented as SEQ ID NO: 242, SEQ ID NO: 243, and SEQ ID NO: 244, respectively, and the HCDR1, HCDR2, and HCDR3 regions are presented as SEQ ID NO: 250, SEQ ID NO: 251, and SEQ ID NO: 252, respectively.

Example 2: Humanization of Murine Marburg mAb

[1130] Humanization of CAN30G5

[1131] Human germline heavy and light chain variable domains with maximum identity alignment with the murine sequences were identified in the NCBI databases for use as identify acceptor frameworks. The human germline alleles selected were IGHV3-73-01/IGHJ4-01 (VH chain) and IGKV2-30-02/IGKJ2-02 (VK chain). These human germline alleles were identified as best matching and used as an acceptor framework for grafting the CDRs. All 6 CDRs (SEQ ID NOs: 63-65 and 51-53) corresponding to heavy and light chains were inserted into the human framework regions to encode complementarity determining regions for heavy and light chains (SEQ ID NOs: 254-256 and 262-264). The cdrCAN30G5 VL and VH regions are presented as SEQ ID NOs: 49 and 50 (nucleotide and amino acid sequences of cdrCAN30G5 VL) and SEQ ID NOs: 61 and 62 (nucleotide and amino acid sequences of cdrCAN30G5 VH).

[1132] Surface exposure and/or involvement in folding or interchain contacts were determined and residues were changed or maintained based on these determinations. Antibodies huCAN30G5 and rehuCAN30G5 "Human engineered" were generated by identifying the closest human germline allele for CAN30G5 mAbs VH and Vk, individually. These were then designed for use as acceptor frameworks, resulting in the VH and VL sequences of huCAN30G5. These sequences are presented as SEQ ID NOs: 1 and 2 (nucleotide and amino acid sequences of huCAN30G5 VL, respectively) and SEQ ID NOs: 13 and 14 (nucleotide and amino acid sequences of huCAN30G5 VH, respectively). The rehuCAN9G1 mAb was further resurfaced by substitution(s) made on surface exposed amino acids to correspond to the adopted human frameworks without disruption of the CDRs. These sequences are presented as SEQ ID NOs: 25 and 26 (nucleotide and amino acid sequences of rehuCAN30G5 VL) and SEQ ID NOs: 37 and 38 (nucleotide and amino acid sequences of rehuCAN30G5 VH).

[1133] Humanization of CAN40G1

[1134] The humanized IgG1/k versions of the CAN40G1 murine mAb were created as above for CAN30G5. The human germline alleles selected were IGHV1-2-02/IGHJ4-01 (VH chain) and IGKV4-1-01/IGKJ2-0 (VK chain). All 6 CDRs (SEQ ID NOs: 135-137 and 123-125) corresponding to heavy and light chains were inserted into the human framework regions to encode complementarity determining regions for heavy and light chains (SEQ ID NOs: 138-140 and 126-128). The cdrCAN40G1 VL and VH regions are presented as SEQ ID NOs: 121 and 122 (nucleotide and amino acid sequences of cdrCAN40G1 VL) and SEQ ID NOs: 133 and 134 (nucleotide and amino acid sequences of cdrCAN40G1 VH). The huCAN40G1 sequences are presented as SEQ ID NOs: 73 and 74 (nucleotide and amino acid

sequences of huCAN40G1 VL) and SEQ ID NOs: 85 and 86 (nucleotide and amino acid sequences of huCAN40G1 VH). The rehuCAN40G1 sequences are presented as SEQ ID NOs 97 and 98 (nucleotide and amino acid sequences of rehuCAN40G1 VL) and SEQ ID NOs 109 and 110 (nucleotide and amino acid sequences of rehuCAN40G1 VH).

[1135] Humanization of CAN54G2

[1136] The humanized IgG1/k versions of the CAN54G2 murine mAb were created as above for CAN30G5. The human germline alleles selected were IGHV1-46-01/ IGHJ4-01 (VH chain) and IGKV2-30-02/ IGKJ2-02 (VK chain). All 6 CDRs (SEQ ID NOs: 207-209 and 195-197) corresponding to heavy and light chains were inserted into the human framework regions to encode complementarity determining regions for heavy and light chains (SEQ ID NOs: 66-68 and 54-56). The cdrCAN54G2 VL and VH regions are presented as SEQ ID NOs: 193 and 194 (nucleotide and amino acid sequences of cdrCAN54G2 VL) and SEQ ID NOs: 205 and 206 (nucleotide and amino acid sequences of cdrCAN54G2 VH). The huCAN54G2 sequences are presented as SEQ ID NOs: 145 and 146 (nucleotide and amino acid sequences of huCAN54G2 VL) and SEQ ID NOs: 157 and 158 (nucleotide and amino acid sequences of huCAN54G2 VH). The rehuCAN54G2 sequences are presented as SEQ ID NOs: 169 and 170 (nucleotide and amino acid sequences of rehuCAN54G2 VL) and SEQ ID NOs: 181 and 182 (nucleotide and amino acid sequences of rehuCAN54G2 VH).

Example 3: Transient Expression and Purification of Humanized Marburg mAbs

[1137] The VH and VL regions for the humanized Marburg mAbs described in Example 2 (cdrCAN30G5, huCAN30G5, rehuCAN30G5, cdrCAN40G1, huCAN40G1, rehuCAN40G1, cdrCAN54G2, huCAN54G2, and rehuCAN54G2) were cloned into vectors for expression as full-sized humanized antibodies having human IgG constant regions. The VH and VL regions of the parent murine antibody (CAN30G5, CAN40G1, and CAN54G2) were also cloned into human constant region vectors for expression as mouse-human chimeric antibodies.

[1138] Humanized Marburg mAbs were produced by transient transfections in 293F, CHO-S or CHOK1S-V cells. One day prior to transfection, 293F, CHO-S or CHOK1S-V cells were counted using a Haemocytometer in the presence of Trypan Blue, then passaged into transfection medium (293F cells remained in FreeStyle 293 Expression medium; CHO cells were transferred into DMEM/F12 supplemented with 10% FBS and L-Glutamine) at a concentration of $6-8 \times 10^5$ cells/ml and incubated 24 hours at 37°C, 8% CO₂ and in a shaking

incubator at 100 rpm. Freestyle Max Transfection Agent was diluted 1/16 in Optimem before being added to 312.5 µg of the appropriate DNA also diluted in Optimem. DNA/Freestyle Max Transfection Agent mix was incubated at room temperature for 20 minutes and added to 250 x 10⁶ cells in FreeStyle 293 Expression Medium (no DMSO) for 293F cells or DMEM/F12 + 10% FBS + 5 mM L-Glutamine that had been treated for 3 hours with 1% DMSO for CHO cells.

[1139] The culture was harvested after incubation at 37°C/5% CO₂/125 rpm in a shaking incubator by centrifuging the culture at 1455 x g for 30 minutes, removing the supernatant and filtering it through a 0.22 µm bottle top filter. The supernatant was concentrated by spin cell concentrator equipped with a 50 kDa membrane to a final volume of ~100 mL. The concentrated supernatant was purified by Protein G purification on the FPLC or by using Protein G GraviTrap columns (manual purification system). The purified sample was buffer exchanged by spin-cell concentrator equipped with a 50 kDa membrane into D-PBS and concentrated down to a final volume of 1-2 mL. The final protein concentration was determined by BCA using the Pierce BCA Kit.

Example 4: Screening of Humanized Marburg mAbs

[1140] An ELISA was performed to test the binding of the humanized Marburg mAbs described in Example 3 against multiple strains of Marburg GP (Musoke, Ravn or Angola) or derivatives thereof (GPe, GP ectodomain; GPeΔmuc, GPe with mucin domain removed; GPeΔmucAtm, GPe with both mucin and transmembrane domains removed) and to determine if they are cross-reactive to various strains of Ebola virus (EBOV) GP or derivatives thereof (GPe, GPeΔmuc, GPeΔmucAtm). The ELISA plate was coated with 200ng/well of antigen. The wells were blocked with 5% skim milk then probed with 60 µl serially diluted humanized mAbs starting at (17.0ug/mL to 2.1ug/mL). After washing plates, binding was detected with commercial goat anti-human HRP conjugate antibody. Where appropriate, development and detection were carried out with anti-murine HRP-conjugated secondary Abs at the appropriate dilution for positive controls, murine mAbs, and negative (IgG Control mAb) controls were also run. The plate was read at 405nm after minimum 15 minutes incubation at room temperature (RT) with ABTS substrate.

[1141] . Results: huCAN30G5, huCAN40G1 and huCAN54G2 were tested for binding by ELISA to MARV Ravn, MARV Angola and MARV Musoke GPe, along with the murine versions (muCAN30G5, muCAN40G1 and muCAN54G2). Table 3 lists the ELISA results in

table form. The results show both murine and humanized versions of CAN40G1, and CAN54G2 bind and recognize all of the MARV GPe's. Murine and humanized versions of CAN30G5 bind and recognize only the MARV Ravn GPe.

Table 3: ELISA Results of anti-MARV humanized and murine mAbs vs. MARV Glycoproteins

Glycoprotein (GP)	mAb @ 2ug/mL	OD ₄₀₅ @ 30 min
MARV Ravn	muCAN30G5	0.160
	huCAN30G5	2.740
	muCAN40G1	0.504
	huCAN40G1	2.753
	muCAN54G2	0.160
	huCAN54G2	0.890
	IgG Neg Control (murine)	0.049
	IgG Neg Control (human)	0.052
MARV Angola	muCAN40G1	0.857
	huCAN40G1	3.825
	muCAN54G2	0.150
	huCAN54G2	0.502
	IgG Neg Control (murine)	0.047
	IgG Neg Control (human)	0.054
MARV Musoke	muCAN40G1	0.536
	huCAN40G1	2.735
	muCAN54G2	0.185
	huCAN54G2	0.908
	IgG Neg Control (murine)	0.049
	IgG Neg Control (human)	0.056

Example 5: Western Blots of Humanized Marburg mAbs

[1142] A 4-12% gradient SDS-PAGE gel is run for 1.5 hours at 200 volts with a combination of MARV and EBOV GP proteins. The gel is then transferred to a nitrocellulose membrane for a minimum of 1 hour at 45 volts. The membrane is blocked overnight at 4°C with 5% skim milk in 1xTBST. The next day the humanized Ebola mAbs (1°Ab) described in Example 3 are diluted in 2.5% skim milk in 1xTBST at concentrations ranging from 2 µg/mL to 5 µg/mL depending on the antibody and used to probe the membrane containing the transferred proteins for 2 hours at room temperature (RT). The membranes are then washed

with 1xTBST to remove unbound 1°Ab and probed with anti-human IgG-HRP (2°Ab) at a dilution of 1:4000 to 1:5000 for 1.5 hours at RT. Where appropriate, development and detection are carried out with anti-murine HRP-conjugated secondary Abs at the appropriate dilution for controls.

Example 6: Pseudovirus Neutralization Assay

[1143] The humanized Marburg mAbs described in Example 3 are tested for neutralization of recombinant Vesicular stomatitis virus (VSV) pseudotyped with MARV GP. VSV pseudovirions containing a GFP gene in place of the VSV G gene (VSVΔG) and bearing the glycoprotein of MARV are generated as previously described (Takeda, A. et al. Proc Natl Acad Sci USA, 1997. 94(26): 14764-14769). Experiments are performed in triplicate with VSVΔG bearing either full-length MARV GP (VSVΔG-GP) or mucin-deleted Δ257-425 GP (VSVΔG-GPΔmuc). Pseudovirions are incubated with anti-VSV G mAb for 1 hour at RT, then incubated with 2.5, 10 or 50 μg/mL of each humanized Marburg mAb in DMEM-10%FBS for an additional hour. Pseudovirion/mAb complexes are added to Vero cells at a multiplicity of infection (MOI) of 0.01. After 48 hours, infection was evaluated by counting GFP-expressing cells.

Example 7: Mouse in vivo Protection Experiments

[1144] All procedures with infectious marburgviruses are performed in biosafety level 4 facilities under IACUC-approved protocols. One hour pre- or post-exposure, BALB/c mice are treated intraperitoneally (IP) with purified humanized Ebola mAbs described in Example 3, non-relevant IgG, or PBS alone. The mice are then challenged IP with 1000 plaque-forming units (p.f.u.) mouse-adapted MARV. Mice are monitored for clinical signs of infections for 28 days post-exposure at which point the study ends and the mice are euthanized.

What is claimed is:

1. An isolated antibody or antigen-binding portion thereof that binds to a filovirus, wherein the antibody or antigen-binding portion thereof comprises:
 - a) a light chain CDR1 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NO: 6, 78, or 150;
 - b) a light chain CDR2 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NO: 7, 79, or 151;
 - c) a light chain CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NO: 8, 80 or 152;
 - d) a heavy chain CDR1 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NO: 18, 90, or 162;
 - e) a heavy chain CDR2 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NO: 19, 91, or 163;
 - f) a heavy chain CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NO: 20, 92, and 164;
 - g) a light chain FR1 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NO: 333, 349, 357, 373, or 381;
 - h) a light chain FR2 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NO: 334, 342, 350, 358, 374, 382;
 - i) a light chain FR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NO: 335, 343, 351, 359, 367, 375, 383, or 391;
 - j) a light chain FR4 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NO: 336, 344, 360, 368, or 376;
 - k) a heavy chain FR1 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NOs: 337, 361, 369, 377, 385, or 393;
 - l) a heavy chain FR2 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NO: 338, 346, 354, 362, 378, 386, 394, or 402;

- m) a heavy chain FR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NO: 339, 347, 355, 363, 371, 379, 387, 395 or 403; and,
- n) a heavy chain FR4 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NO: 340 or 372.

2. The isolated antibody or antigen-binding portion thereof of claim 1, wherein the antibody or antigen-binding portion thereof comprises:

- a) a light chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NOs: 6, 7 and 8, respectively; a heavy chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NOs: 18, 19 and 20, respectively; a light chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NOs: 333, 334, 335 and 336, respectively; and a heavy chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NOs: 337, 338, 339, and 340, respectively;
- b) a light chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NOs: 30, 31, and 32, respectively; a heavy chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NOs: 42, 43, and 44, respectively; a light chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NOs: 341, 342, 343, and 344, respectively; and a heavy chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NOs: 345, 346, 347, and 348, respectively;
- c) a light chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NOs: 54, 55, and 56, respectively; a heavy chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NOs: 66, 67, and 68, respectively; a

- light chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NOs: 349, 350, 351, and 352, respectively; and a heavy chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NOs: 353, 354, 355, and 356, respectively;
- d) a light chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NOs: 78, 79 and 80, respectively; a heavy chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NOs: 90, 91 and 92, respectively; a light chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NOs: 357, 358, 359 and 360, respectively; and a heavy chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NOs: 361, 362, 363, and 364, respectively;
- e) a light chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NOs: 102, 103, and 104, respectively; a heavy chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NOs: 114, 115, and 116, respectively; a light chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NOs: 365, 366, 367, and 368, respectively; and a heavy chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NOs: 369, 370, 371, and 372, respectively;
- f) a light chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NOs: 126, 127, and 128, respectively; a heavy chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NOs: 138, 139, and 140, respectively; a light chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at

- least about 85% sequence identity to an amino acid sequence comprising SEQ ID NOs: 373, 374, 375, and 376, respectively; and a heavy chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NOs: 377, 378, 379, and 380, respectively;
- g) a light chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NOs: 150, 151, and 152, respectively; a heavy chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NOs: 162, 163, and 164, respectively; a light chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NOs: 381, 382, 383, and 384, respectively; and a heavy chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NOs: 385, 386, 387 and 388, respectively;
- h) a light chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NOs: 174, 175, and 176, respectively; a heavy chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NOs: 186, 187, and 188, respectively; a light chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NOs: 389, 390, 391, and 392, respectively; and a heavy chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NOs: 393, 394, 395, and 396, respectively; or
- i) a light chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NOs: 198, 199 and 200, respectively; a heavy chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NOs: 210, 211, and 212, respectively; a light chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID

NOs: 397, 398, 399, and 400, respectively; and a heavy chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence comprising SEQ ID NOs: 401, 402, 403 and 404, respectively.

3. An isolated antibody or antigen-binding portion thereof that binds to a filovirus, wherein the antibody or antigen-binding portion thereof comprises:

- a) a light chain CDR1 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NO: 3, 75, or 147;
- b) a light chain CDR2 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NO: 4, 76, or 148;
- c) a light chain CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NO: 5, 77, or 149;
- d) a heavy chain CDR1 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NOs: 15, 87, or 159;
- e) a heavy chain CDR2 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NOs: 16, 88, or 160;
- f) a heavy chain CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NO: 17, 89, or 161;
- g) a light chain FR1 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NO: 9, 57, 81, 129, or 153;
- h) a light chain FR2 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NO: 10, 34, 58, 82, 130, or 154;
- i) a light chain FR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NO: 11, 35, 59, 83, 107 131, 155, or 179;

- j) a light chain FR4 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NO: 12, 36, 60, 84, 108, or 132;
 - k) a heavy chain FR1 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NOs: 21, 93, 117, 141, 165, or 189;
 - l) a heavy chain FR2 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NO: 22, 46, 70, 94, 142, 166, 190 or 214;
 - m) a heavy chain FR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NOs: 23, 47, 71, 95, 119, 143, 167, 191 or 215; and,
 - n) a heavy chain FR4 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NOs: 24, 48, or 120.
4. The isolated antibody or antigen-binding portion thereof of claim 3, wherein the antibody or antigen-binding portion thereof comprises:
- a) a light chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NOs: 3, 4, and 5, respectively; a heavy chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NOs: 15, 16, and 17, respectively; a light chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NOs: 9, 10, 11, and 12, respectively; and a heavy chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NOs: 21, 22, 23, and 24, respectively;
 - b) a light chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NOs: 27, 28, and 29, respectively; a heavy chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least

- about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NOs: 39, 40, and 41, respectively; a light chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NOs: 33, 34, 35, and 36, respectively; and a heavy chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NOs: 45, 46, 47 and 48, respectively;
- c) a light chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NOs: 51, 52, and 53, respectively; a heavy chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NOs: 63, 64, and 65, respectively; a light chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NOs: 57, 58, 59 and 60, respectively; and a heavy chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NOs: 69, 70, 71, and 72, respectively;
- d) a light chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NOs: 75, 76, and 77, respectively; a heavy chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NOs: 87, 88, and 89, respectively; a light chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NOs: 81, 82, 83, and 84, respectively; and a heavy chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NOs: 93, 94, 95, and 96, respectively;
- e) a light chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a

- nucleotide sequence comprising SEQ ID NOs: 99, 100, and 101, respectively; a heavy chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NOs: 111, 112, and 113, respectively; a light chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NOs: 105, 106, 107, and 108, respectively; and a heavy chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NOs: 117, 118, 119, and 120, respectively;
- f) a light chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NOs: 123, 124 and 125, respectively; a heavy chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NOs: 135, 136, and 137, respectively; a light chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NOs: 129, 130, 131, and 132, respectively; and a heavy chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NOs: 141, 142, 143, and 144, respectively;
- g) a light chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NOs: 147, 148 and 149, respectively; a heavy chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NOs: 159, 160, and 161, respectively; a light chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NOs: 153, 154, 155, and 156, respectively; and a heavy chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NOs: 165, 166, 167, and 168, respectively;

- h) a light chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NOs: 171, 172, and 173, respectively; a heavy chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NOs: 183, 184, and 185, respectively; a light chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NOs: 177, 178, 179 and 180, respectively; and a heavy chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NOs: 189, 190, 191, and 192, respectively; or
- i) a light chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NOs: 195, 196 and 197, respectively; a heavy chain CDR1, CDR2, and CDR3 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NOs: 207, 208, and 209, respectively; a light chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NOs: 201, 202, 203 and 204, respectively; and a heavy chain FR1, FR2, FR3, and FR4 comprising an amino acid sequence that has at least about 85% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NOs: 213, 214, 215 and 216, respectively.

5. An isolated antibody or antigen-binding portion thereof that binds to a filovirus, wherein the antibody or antigen-binding portion thereof comprises:

- a) a variable heavy chain comprising an amino acid sequence that has at least about 98% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NO: 13, 37, 61, 85, 109, 133, 157, 181, or 205; and
- b) a variable light chain comprising an amino acid sequence that has at least about 98% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NO: 1, 25, 49, 73, 97, 121, 145, 169, or 193.

6. The antibody or antigen-binding portion thereof of claim 5, wherein the antibody of antigen-binding portion thereof comprises:

- a) a variable heavy chain comprising an amino acid sequence that has at least about 98% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NO: 13 and a variable light chain comprising an amino acid sequence that has at least about 98% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NO: 1;
- b) a variable heavy chain comprising an amino acid sequence that has at least about 98% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NO: 37 and a variable light chain comprising an amino acid sequence that has at least about 98% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NO: 25;
- c) a variable heavy chain comprising an amino acid sequence that has at least about 98% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NO: 61 and a variable light chain comprising an amino acid sequence that has at least about 98% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NO: 49;
- d) a variable heavy chain comprising an amino acid sequence that has at least about 98% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NO: 85 and a variable light chain comprising an amino acid sequence that has at least about 98% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NO: 73;
- e) a variable heavy chain comprising an amino acid sequence that has at least about 98% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NO: 109 and a variable light chain comprising an amino acid sequence that has at least about 98% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NO: 97;
- f) a variable heavy chain comprising an amino acid sequence that has at least about 98% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NO: 133 and a variable light chain comprising an amino acid sequence that has at least about 98% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NO: 121;

- g) a variable heavy chain comprising an amino acid sequence that has at least about 98% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NO: 157 and a variable light chain comprising an amino acid sequence that has at least about 98% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NO: 145;
 - h) a variable heavy chain comprising an amino acid sequence that has at least about 98% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NO: 181 and a variable light chain comprising an amino acid sequence that has at least about 98% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NO: 169; or
 - i) a variable heavy chain comprising an amino acid sequence that has at least about 98% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NO: 205 and a variable light chain comprising an amino acid sequence that has at least about 98% sequence identity to an amino acid sequence encoded by a nucleotide sequence comprising SEQ ID NO: 193.
7. An isolated antibody or antigen-binding portion thereof that binds to a filovirus, wherein the antibody or antigen-binding portion thereof comprises:
- a) a variable heavy chain comprising an amino acid sequence that has at least about 98% sequence identity to SEQ ID NO: 14, 38, 62, 86, 110, 134, 158, 182, or 206; and
 - b) a variable light chain comprising an amino acid sequence that has at least about 98% sequence identity to SEQ ID NO: 2, 26, 50, 74, 98, 122, 146, 170 or 194.
8. The isolated antibody or antigen-binding portion of claim 7, wherein the antibody or antigen-binding portion thereof comprises:
- a) a variable heavy chain comprising an amino acid sequence that has at least about 98% sequence identity to SEQ ID NO: 14 and a variable light chain comprising an amino acid sequence that has at least about 98% sequence identity to SEQ ID NO: 2;
 - b) a variable heavy chain comprising an amino acid sequence that has at least about 98% sequence identity to SEQ ID NO: 38 and a variable light chain comprising an amino acid sequence that has at least about 98% sequence identity to SEQ ID NO: 26;
 - c) a variable heavy chain comprising an amino acid sequence that has at least about 98% sequence identity to SEQ ID NO: 62 and a variable light chain comprising an amino acid sequence that has at least about 98% sequence identity to SEQ ID NO: 50;

- d) a variable heavy chain comprising an amino acid sequence that has at least about 98% sequence identity to SEQ ID NO: 86 and a variable light chain comprising an amino acid sequence that has at least about 98% sequence identity to SEQ ID NO: 74;
 - e) a variable heavy chain comprising an amino acid sequence that has at least about 98% sequence identity to SEQ ID NO: 110 and a variable light chain comprising an amino acid sequence that has at least about 98% sequence identity to SEQ ID NO: 98;
 - f) a variable heavy chain comprising an amino acid sequence that has at least about 98% sequence identity to SEQ ID NO: 134 and a variable light chain comprising an amino acid sequence that has at least about 98% sequence identity to SEQ ID NO: 122;
 - g) a variable heavy chain comprising an amino acid sequence that has at least about 98% sequence identity to SEQ ID NO: 158 and a variable light chain comprising an amino acid sequence that has at least about 98% sequence identity to SEQ ID NO: 146;
 - h) a variable heavy chain comprising an amino acid sequence that has at least about 98% sequence identity to SEQ ID NO: 182 and a variable light chain comprising an amino acid sequence that has at least about 98% sequence identity to SEQ ID NO: 170; or
 - i) a variable heavy chain comprising an amino acid sequence that has at least about 98% sequence identity to SEQ ID NO: 206 and a variable light chain comprising an amino acid sequence that has at least about 98% sequence identity to SEQ ID NO: 194.
9. The isolated antibody or antigen-binding portion of claim 8, wherein the antibody or antigen-binding portion thereof comprises:
- a) a variable heavy chain comprising an amino acid sequence comprising SEQ ID NO: 14 and a variable light chain comprising an amino acid sequence comprising SEQ ID NO: 2;
 - b) a variable heavy chain comprising an amino acid sequence comprising SEQ ID NO: 38 and a variable light chain comprising an amino acid sequence comprising SEQ ID NO: 26;
 - c) a variable heavy chain comprising an amino acid sequence comprising SEQ ID NO: 62 and a variable light chain comprising an amino acid sequence comprising SEQ ID NO: 50;
 - d) a variable heavy chain comprising an amino acid sequence comprising SEQ ID NO: 86 and a variable light chain comprising an amino acid sequence comprising SEQ ID NO: 74;

- e) a variable heavy chain comprising an amino acid sequence comprising SEQ ID NO: 110 and a variable light chain comprising an amino acid sequence comprising SEQ ID NO: 98;
- f) a variable heavy chain comprising an amino acid sequence comprising SEQ ID NO: 134 and a variable light chain comprising an amino acid sequence comprising SEQ ID NO: 122;
- g) a variable heavy chain comprising an amino acid sequence comprising SEQ ID NO: 158 and a variable light chain comprising an amino acid sequence comprising SEQ ID NO: 146;
- h) a variable heavy chain comprising an amino acid sequence comprising SEQ ID NO: 182 and a variable light chain comprising an amino acid sequence comprising SEQ ID NO: 170; or
- i) a variable heavy chain comprising an amino acid sequence comprising SEQ ID NO: 206 and a variable light chain comprising an amino acid sequence comprising SEQ ID NO: 194.

10. The isolated antibody or antigen-binding portion thereof of any one of the preceding claims, wherein the antibody or antigen-binding portion is selected from the group consisting of: (i) a whole immunoglobulin; (ii) an scFv; (iii) a Fab fragment; (iv) an F(ab')₂; and (v) a disulfide linked Fv.

11. The isolated antibody or antigen-binding portion thereof of any one of the preceding claims, wherein the antibody or antigen-binding portion thereof binds to the GP subunit of the filovirus.

12. The isolated antibody or antigen-binding portion thereof of any one of the preceding claims, wherein the antibody or antigen-binding portion thereof binds to the mucin domain of the GP1 subunit of the filovirus.

13. The isolated antibody or antigen-binding portion thereof of any one of the preceding claims, wherein the antibody or antigen-binding portion thereof binds to the GP2 subunit of the filovirus.

14. The isolated antibody or antigen-binding portion thereof of any one of the preceding claims, wherein the antibody or antigen-binding portion thereof binds to the GP2 wing subunit of the filovirus.
15. The isolated antibody or antigen-binding portion thereof of any one of the preceding claims, wherein the antibody or antigen-binding portion thereof is cross-reactive to at least two filoviruses.
16. The isolated antibody or antigen-binding portion thereof of any one of the preceding claims, wherein the filovirus is *Ebolavirus* or *Marburgvirus*.
17. The isolated antibody or antigen-binding portion thereof of any one of the preceding claims, wherein the filovirus is *Zaire ebolavirus*, *Sudan ebolavirus*, *Reston ebolavirus*, *Tai Forest ebolavirus*, *Cote d'Ivoire ebolavirus* or *Bundibugyo ebolavirus*.
18. A nucleic acid sequence encoding the antibody or antigen-binding portion thereof of any one of claims 1-17.
19. An expression vector comprising a promoter operably linked to a nucleotide sequence of claim 18.
20. An expression vector comprising a nucleotide sequence with the following sequences:
- a) SEQ ID NOs: 3, 4, 5, 9, 10, 11, 12, 15, 16, 17, 21, 22, 23, and 24;
 - b) SEQ ID NOs: 27, 28, 29, 33, 34, 35, 36, 39, 40, 41, 45, 46, 47, and 48;
 - c) SEQ ID NOs: 51, 52, 53, 57, 58, 59, 60, 63, 64, 65, 69, 70, 71, and 72;
 - d) SEQ ID NOs: 75, 76, 77, 81, 82, 83, 84, 87, 88, 89, 93, 94, 95, and 96;
 - e) SEQ ID NOs: 99, 100, 101, 105, 106, 107, 108, 111, 112, 113, 117, 118, 119, and 120,
 - f) SEQ ID NOs: 123, 124, 125, 129, 130, 131, 132, 135, 136, 137, 141, 142, 143, and 144;
 - g) SEQ ID NOs: 147, 148, 149, 153, 154, 155, 156, 159, 160, 161, 165, 166, 167, and 168;
 - h) SEQ ID NOs: 171, 172, 173, 177, 178, 179, 180, 183, 184, 185, 189, 190, 191, and 192; or

- i) SEQ ID NOs: 195, 196, 197, 201, 202, 203, 204, 207, 208, 209, 213, 214, 215 and 216.
21. An expression vector comprising a nucleotide sequence with the following sequences:
- a) SEQ ID NOs: 1 and 13;
 - b) SEQ ID NOs: 25 and 37;
 - c) SEQ ID NOs: 49 and 61;
 - d) SEQ ID NOs: 73 and 85;
 - e) SEQ ID NOs: 97 and 109;
 - f) SEQ ID NOs: 121 and 133;
 - g) SEQ ID NOs: 145 and 157;
 - h) SEQ ID NOs: 169 and 181; or
 - i) SEQ ID NOs: 193 and 205.
22. A host cell comprising the expression vector of any one of claims 19-21.
23. The host cell of claim 22, wherein the cell is a bacterial, eukaryotic or mammalian cell.
24. The host cell of claim 22 or 23, wherein the cell is COS-1, COS-7, HEK293, BHK21, CHO, BSC-1, HepG2, SP2/0, HeLa, myeloma or lymphoma cell.
25. A method of producing an antibody or antigen-binding portion thereof that binds to a filovirus comprising:
- a) culturing a host cell of any one of claims 22-24; and
 - b) recovering the antibody or antigen-binding portion thereof.
26. A pharmaceutical composition comprising the antibody or antigen-binding portion thereof of any one of claims 1-17 and a pharmaceutically acceptable carrier.
27. A composition comprising the antibody or antigen-binding portion thereof of any one of claims 1-17 and one or more other antibodies or antigen-binding portions thereof, wherein the one or more other antibodies or antigen-binding portions thereof binds a protein produced by a virus in the *Filoviridae* family.

28. The composition of claim 27, wherein the protein is a glycoprotein.
29. The composition of claim 27 or 28, wherein the virus is *Ebolavirus* or *Marburgvirus*.
30. The composition of claim 29, wherein the virus is *Zaire ebolavirus*, *Sudan ebolavirus*, *Reston ebolavirus*, *Tai Forest ebolavirus*, *Bundibugyo ebolavirus*, *Cote d'Ivoire ebolavirus*, Marburg virus or Ravn virus.
31. The composition of any one of claims 27-30, further comprising a pharmaceutically acceptable carrier.
32. A method for ameliorating, treating or preventing a filovirus infection in a subject in need thereof, the method comprising administering to the subject a therapeutically effective amount of the antibody or antigen-binding portion thereof of any one of claims 1-17.
33. A method for ameliorating, treating or preventing a filovirus infection in a subject in need thereof, the method comprising administering to the subject a therapeutically effective amount of the composition of any one of claims 26-31.
34. The method of claim 32 or 33, wherein the subject is a human.
35. A method for detecting *Marburgvirus* in a sample, the method comprising contacting the sample with the antibody or antigen-binding portion thereof of any one of claims 1-13.
32. The method of claim 35, wherein the sample is a cell, tissue, or biological fluid from a subject suspected of having or at risk of a filovirus infection.
33. An expression vector comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs: 1, 13, 25, 37, 49, 61, 73, 85, 97, 109, 121, 133, 145, 157, 169, 181, 193, and 205.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/CA2016/000040

A. CLASSIFICATION OF SUBJECT MATTER

IPC: **C12N 15/13** (2006.01), **A61K 39/42** (2006.01), **A61P 31/12** (2006.01), **C07K 16/10** (2006.01), **C07K 16/46** (2006.01), **C12N 15/63** (2006.01), **C12N 5/10** (2006.01), **C12P 21/08** (2006.01), **G01N 33/569** (2006.01)

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
All IPCs

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic database(s) consulted during the international search (name of database(s) and, where practicable, search terms used)
Questel Orbit, Scopus, GenomeQuest, Keywords: filovirus, antibody, monoclonal, Authors: JOHNSTONE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	HEVEY, M. et al., "Characterization of monoclonal antibodies to Marburg virus (strain Musoke) glycoprotein and identification of two protective epitopes", <i>Virology</i> , Vol. 314, No 1, 15 September 2003 (15-09-2003), pages 350-357, ISSN: 0042-6822, doi:10.1016/S0042-6822(03)00416-1. The whole document.	1-31 and 35-37
A	MARCEAU, C.D. et al., "Novel neutralizing monoclonal antibodies protect rodents against lethal filovirus challenges", <i>Trials in Vaccinology</i> , Vol. 3, No. 1, pages: 89-94, December 2014 (12-2014), doi:10.1016/j.trivac.2014.04.002. The whole document.	1-31 and 35-37
P,X	WO2015/127140 A2 (BERRY, J. and SAPHIRE, E.) 27 August 2015 (27-08-2015). The whole document.	1-31 and 35-37
P,X	WO2015/123777 A1 (BERRY, J. and NYKIFORUK, C.) 27 August 2015 (27-08-2015). The whole document.	1-31 and 35-37

☐ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

* "A" "E" "L" "O" "P"	Special categories of cited documents: document defining the general state of the art which is not considered to be of particular relevance earlier application or patent but published on or after the international filing date document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) document referring to an oral disclosure, use, exhibition or other means document published prior to the international filing date but later than the priority date claimed	"T" "X" "Y" "&"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art document member of the same patent family
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Date of the actual completion of the international search
01 June 2016 (01-06-2016)

Date of mailing of the international search report
01 June 2016 (01-06-2016)

Name and mailing address of the ISA/CA
Canadian Intellectual Property Office
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INTERNATIONAL SEARCH REPORT

International application No.

PCT/CA2016/000040**Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of the first sheet)**

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claim Nos.: 32-34
because they relate to subject matter not required to be searched by this Authority, namely:
Claims 32-34 are directed to a method for treatment of the human or animal body by surgery or therapy, which the International Searching Authority is not required to search under PCT Rule 39.1(iv). However, this Authority has carried out a search based on the alleged effect or purpose/use of the antibody or antigen-binding portion thereof of any one of claims 1-17 or a composition comprising said antibody or antigen-binding portion thereof.
2. ☐ Claim Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claim Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

See extra sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☒ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claim Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claim Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.

Continuation of Box III:

The claims are directed to a plurality of inventive concepts as follows:

Group A - Claims 1-37 (all partially) are directed to an antibody that specifically binds a filovirus and comprising the CDRs of antibody CAN30G5, a nucleic acid, a vector, a host cell, a pharmaceutical composition and methods, all relating to said antibody;

Group B - Claims 1-37 (all partially) are directed to same subject matter of Group A but relating to the CDRS of antibody CAN40G1; and

Group C - Claims 1-37 (all partially) are directed to same subject matter of Group A but relating to the CDRS of antibody CAN54G2.

The only linking feature between the different groups is an antibody that specifically binds a filovirus. Said concept is known in the prior art (see D1 and D2). Thus, the claims must be limited to one inventive concept as set out in PCT Rule 13.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.

PCT/CA2016/000040

Patent Document Cited in Search Report	Publication Date	Patent Family Member(s)	Publication Date
WO2015127140A2	27 August 2015 (27-08-2015)	WO2015127140A2 WO2015127140A3 WO2015123777A1	27 August 2015 (27-08-2015) 01 October 2015 (01-10-2015) 27 August 2015 (27-08-2015)
WO2015123777A1	27 August 2015 (27-08-2015)	WO2015123777A1 WO2015127140A2 WO2015127140A3	27 August 2015 (27-08-2015) 27 August 2015 (27-08-2015) 01 October 2015 (01-10-2015)