

HVR-H3 comprising the amino acid sequence of SEQ ID NO: 17, (d) HVR-L1 comprising the amino acid sequence of SEQ ID NO: 22, (e) HVR-L2 comprising the amino acid sequence of SEQ ID NO: 25 and (f) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 29; (vii) (a) HVR-H1 comprising the amino acid sequence of SEQ ID NO: 12, (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO: 15, (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO: 20, (d) HVR-L1 comprising the amino acid sequence of SEQ ID NO: 23, (e) HVR-L2 comprising the amino acid sequence of SEQ ID NO: 26 and (f) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 30; or (viii) (a) HVR-H1 comprising the amino acid sequence of SEQ ID NO: 12, (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO: 15, (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO: 20, (d) HVR-L1 comprising the amino acid sequence of SEQ ID NO: 21, (e) HVR-L2 comprising the amino acid sequence of SEQ ID NO: 24 and (f) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 27, wherein the antibody further comprises a variant Fc region comprising Ala at position 234, Ala at position 235 and further amino acid alterations of any one of the following (a)-(c): (a) positions 267, 268, and 324; (b) positions 236, 267, 268, 324, and 332; and (c) positions 326 and 333; according to EU numbering.

In another aspect, there is provided an isolated antibody, comprising (a) a VH sequence having the amino acid sequence of any one of SEQ ID NOs: 2-6; (b) a VL sequence having the amino acid sequence of any one of SEQ ID NOs: 8-10; or (c) a VH sequence of any one of SEQ ID NOs: 2-6 and a VL sequence of any one of SEQ ID NOs: 7-10, wherein the antibody further comprises a variant Fc region comprising Ala at position 234, Ala at position 235 and further amino acid alterations of any one of the following (a)-(c): (a) positions 267, 268, and 324; (b) positions 236, 267, 268, 324, and 332; and (c) positions 326 and 333; according to EU numbering.

In one example, there is provided an isolated antibody that binds to dengue virus (DENV) E protein, wherein the antibody comprises: (a) VH comprising the amino acid sequence of SEQ ID NO: 2, VL comprising the amino acid sequence of SEQ ID NO: 7, CH comprising the amino acid sequence of SEQ ID NO: 46 and CL comprising the amino acid sequence of SEQ ID NO: 60, (b) VH comprising the amino acid sequence of SEQ ID NO: 3, VL comprising the amino acid sequence of SEQ ID NO: 7, CH comprising the amino acid sequence of SEQ ID NO: 46 and CL comprising the amino acid sequence of SEQ ID NO: 60, (c) VH comprising the amino acid sequence of SEQ ID NO: 3, VL comprising the amino acid sequence of SEQ ID NO: 7, CH comprising the amino acid sequence of SEQ ID

NO: 54 and CL comprising the amino acid sequence of SEQ ID NO: 60, (d) VH comprising the amino acid sequence of SEQ ID NO: 3, VL comprising the amino acid sequence of SEQ ID NO: 7, CH comprising the amino acid sequence of SEQ ID NO: 59 and CL comprising the amino acid sequence of SEQ ID NO: 60, (e) VH comprising the amino acid sequence of SEQ ID NO: 4, VL comprising the amino acid sequence of SEQ ID NO: 7, CH comprising the amino acid sequence of SEQ ID NO: 46 and CL comprising the amino acid sequence of SEQ ID NO: 60, (f) VH comprising the amino acid sequence of SEQ ID NO: 5, VL comprising the amino acid sequence of SEQ ID NO: 7, CH comprising the amino acid sequence of SEQ ID NO: 46 and CL comprising the amino acid sequence of SEQ ID NO: 60, (g) VH comprising the amino acid sequence of SEQ ID NO: 3, VL comprising the amino acid sequence of SEQ ID NO: 8, CH comprising the amino acid sequence of SEQ ID NO: 46 and CL comprising the amino acid sequence of SEQ ID NO: 60, (h) VH comprising the amino acid sequence of SEQ ID NO: 3, VL comprising the amino acid sequence of SEQ ID NO: 9, CH comprising the amino acid sequence of SEQ ID NO: 46 and CL comprising the amino acid sequence of SEQ ID NO: 60, (i) VH comprising the amino acid sequence of SEQ ID NO: 6, VL comprising the amino acid sequence of SEQ ID NO: 10, CH comprising the amino acid sequence of SEQ ID NO: 46 and CL comprising the amino acid sequence of SEQ ID NO: 60, (j) VH comprising the amino acid sequence of SEQ ID NO: 6, VL comprising the amino acid sequence of SEQ ID NO: 10, CH comprising the amino acid sequence of SEQ ID NO: 59 and CL comprising the amino acid sequence of SEQ ID NO: 60, (k) VH comprising the amino acid sequence of SEQ ID NO: 6, VL comprising the amino acid sequence of SEQ ID NO: 7, CH comprising the amino acid sequence of SEQ ID NO: 46 and CL comprising the amino acid sequence of SEQ ID NO: 60, (l) VH comprising the amino acid sequence of SEQ ID NO: 6, VL comprising the amino acid sequence of SEQ ID NO: 7, CH comprising the amino acid sequence of SEQ ID NO: 54 and CL comprising the amino acid sequence of SEQ ID NO: 60, or (m) VH comprising the amino acid sequence of SEQ ID NO: 6, VL comprising the amino acid sequence of SEQ ID NO: 7, CH comprising the amino acid sequence of SEQ ID NO: 59 and CL comprising the amino acid sequence of SEQ ID NO: 60.

In some examples, an isolated anti-DENV antibody as disclosed herein binds to DENV E protein. In some examples, an anti-DENV antibody as disclosed herein comprises:

(a) (i) HVR-H3 comprising the amino acid sequence $GGX_1ALFYDSYTPX_2DX_3GSWWFDP$, wherein X_1 is R or E, X_2 is R or F, X_3 is G, D or L (SEQ ID NO: 42), (ii) HVR-L3 comprising the amino acid sequence $QQFX_1X_2LPIT$, wherein X_1 is D, S or E, X_2 is D or A (SEQ ID NO:

45), and (iii) HVR-H2 comprising the amino acid sequence VINPRGGSX₁X₂SAQKFQG, wherein X₁ is T or R, X₂ is A or R (SEQ ID NO: 41);

(b) (i) HVR-H1 comprising the amino acid sequence SX₁YX₂H, wherein X₁ is N or Y, X₂ is I or M (SEQ ID NO: 40), (ii) HVR-H2 comprising the amino acid sequence

5 VINPRGGSX₁X₂SAQKFQG, wherein X₁ is T or R, X₂ is A or R (SEQ ID NO: 41), and (iii) HVR-H3 comprising the amino acid sequence GGX₁ALFYDSYTPX₂DX₃GSWWFDP, wherein X₁ is R or E, X₂ is R or F, X₃ is G, D or L (SEQ ID NO: 42);

(c) (i) HVR-H1 comprising the amino acid sequence SX₁YX₂H, wherein X₁ is N or Y, X₂ is I or M (SEQ ID NO: 40), (ii) HVR-H2 comprising the amino acid sequence

10 VINPRGGSX₁X₂SAQKFQG, wherein X₁ is T or R, X₂ is A or R (SEQ ID NO: 41), (iii) HVR-H3 comprising the amino acid sequence GGX₁ALFYDSYTPX₂DX₃GSWWFDP, wherein X₁ is R or E, X₂ is R or F, X₃ is G, D or L (SEQ ID NO: 42), (iv) HVR-L1 comprising the amino acid sequence QASQX₁IRX₂YLN, wherein X₁ is D or E, X₂ is K or Q (SEQ ID NO: 43); (v) HVR-L2 comprising the amino acid sequence DASX₁LKX₂, wherein X₁ is N or E, X₂ is T or F (SEQ ID NO: 44); and (vi) HVR-L3 comprising the amino acid sequence QQFX₁X₂LPIT, wherein X₁ is D, S or E, X₂ is D or A (SEQ ID NO: 45); or

(d) (i) HVR-L1 comprising the amino acid sequence QASQX₁IRX₂YLN, wherein X₁ is D or E, X₂ is K or Q (SEQ ID NO: 43); (ii) HVR-L2 comprising the amino acid sequence DASX₁LKX₂, wherein X₁ is N or E, X₂ is T or F (SEQ ID NO: 44); and (iii) HVR-L3

20 comprising the amino acid sequence QQFX₁X₂LPIT, wherein X₁ is D, S or E, X₂ is D or A

WHAT IS CLAIMED IS:

1. An isolated antibody that binds to dengue virus (DENV) E protein, wherein the antibody comprises:

(i) (a) HVR-H1 comprising the amino acid sequence of SEQ ID NO: 11, (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO: 14, (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO: 17, (d) HVR-L1 comprising the amino acid sequence of SEQ ID NO: 21, (e) HVR-L2 comprising the amino acid sequence of SEQ ID NO: 24 and (f) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 27;

(ii) (a) HVR-H1 comprising the amino acid sequence of SEQ ID NO: 11, (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO: 15, (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO: 17, (d) HVR-L1 comprising the amino acid sequence of SEQ ID NO: 21, (e) HVR-L2 comprising the amino acid sequence of SEQ ID NO: 24 and (f) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 27;

(iii) (a) HVR-H1 comprising the amino acid sequence of SEQ ID NO: 11, (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO: 15, (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO: 18, (d) HVR-L1 comprising the amino acid sequence of SEQ ID NO: 21, (e) HVR-L2 comprising the amino acid sequence of SEQ ID NO: 24 and (f) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 27;

(iv) (a) HVR-H1 comprising the amino acid sequence of SEQ ID NO: 11, (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO: 15, (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO: 19, (d) HVR-L1 comprising the amino acid sequence of SEQ ID NO: 43, (e) HVR-L2 comprising the amino acid sequence of SEQ ID NO: 44 and (f) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 45;

(v) (a) HVR-H1 comprising the amino acid sequence of SEQ ID NO: 11, (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO: 15, (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO: 17, (d) HVR-L1 comprising the amino acid sequence of SEQ ID NO: 21, (e) HVR-L2 comprising the amino acid sequence of SEQ ID NO: 25 and (f) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 28;

(vi) (a) HVR-H1 comprising the amino acid sequence of SEQ ID NO: 11, (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO: 15, (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO: 17, (d) HVR-L1 comprising the amino acid sequence of SEQ ID NO: 22, (e) HVR-L2 comprising the amino acid sequence of SEQ ID NO: 25 and (f) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 29;

(vii) (a) HVR-H1 comprising the amino acid sequence of SEQ ID NO: 12, (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO: 15, (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO: 20, (d) HVR-L1 comprising the amino acid sequence of SEQ ID NO: 23, (e) HVR-L2 comprising the amino acid sequence of SEQ ID NO: 26 and (f) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 30; or

(viii) (a) HVR-H1 comprising the amino acid sequence of SEQ ID NO: 12, (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO: 15, (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO: 20, (d) HVR-L1 comprising the amino acid sequence of SEQ ID NO: 21, (e) HVR-L2 comprising the amino acid sequence of SEQ ID NO: 24 and (f) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 27,

wherein the antibody further comprises a variant Fc region comprising Ala at position

234, Ala at position 235 and further amino acid alterations of any one of the following (a)-(c):

(a) positions 267, 268, and 324;

(b) positions 236, 267, 268, 324, and 332; and

(c) positions 326 and 333;

according to EU numbering.

2. An isolated antibody, comprising (a) a VH sequence having the amino acid sequence of any one of SEQ ID NOs: 2-6; (b) a VL sequence having the amino acid sequence of any one of SEQ ID NOs: 8-10; or (c) a VH sequence of any one of SEQ ID NOs: 2-6 and a VL sequence of any one of SEQ ID NOs: 7-10,

wherein the antibody further comprises a variant Fc region comprising Ala at position

234, Ala at position 235 and further amino acid alterations of any one of the following (a)-(c):

(a) positions 267, 268, and 324;

(b) positions 236, 267, 268, 324, and 332; and

(c) positions 326 and 333;

according to EU numbering.

3. The antibody of claim 1 or 2, wherein the variant Fc region comprises amino acids selected from the group consisting of:

- (a) Glu at position 267;
- (b) Phe at position 268;
- 5 (c) Thr at position 324;
- (d) Ala at position 236;
- (e) Glu at position 332;
- (f) Ala, Asp, Glu, Met, or Trp at position 326; and
- (g) Ser at position 333;

10 according to EU numbering.

4. The antibody of any one of claims 1 to 3, wherein the variant Fc region further comprises amino acids selected from the group consisting of:

- (a) Ala at position 434;
- (b) Ala at position 434, Thr at position 436, Arg at position 438, and Glu at
- 15 position 440;
- (c) Leu at position 428, Ala at position 434, Thr at position 436, Arg at position 438, and Glu at position 440; and
- (d) Leu at position 428, Ala at position 434, Arg at position 438, and Glu at
- position 440;

20 according to EU numbering.