(a) a heavy chain immunoglobulin variable region segment comprising:

a CDR1 comprising the sequence D**V**YMS (SEQ ID NO: 3) (or a sequence that differs by no more than, 1, 2, or 3 amino acids therefrom, optionally provided that **V** is unchanged),

a CDR2 comprising the sequence RIDPENGDTKYDPK**L**QG (SEQ ID NO: 4) (or a sequence that differs by no more than, 1, 2, 3, 4, or 5 amino acids therefrom, optionally provided that **L** is unchanged), and

a CDR3 comprising the sequence GWEGFAY (SEQ ID NO: 5) (or a sequence that differs by no more than, 1, 2, or 3 amino acids therefrom);

(b) a light chain variable region segment comprising:

a CDR1 comprising the sequence RASENVDKYGNSFMH (SEQ ID NO: 6) (or a sequence that differs by no more than, 1, 2, 3, 4, or 5 amino acids therefrom),

a CDR2 comprising the sequence RASELQW (SEQ ID NO: 7) (or a sequence that differs by no more than, 1, 2, or 3 amino acids therefrom), and

a CDR3 comprising the sequence QRSNEVPWT (SEQ ID NO: 8) (or a sequence that differs by no more than, 1, 2, or 3 amino acids therefrom).

In an aspect, the present disclosure provides an antibody molecule capable of binding dengue virus, comprising: (a) a heavy chain immunoglobulin variable region segment comprising: a CDR1 comprising the sequence D**V**YMS (SEQ ID NO: 3) or DTYMS (SEQ ID NO: 14), a CDR2 comprising the sequence RIDPENGDTKYDPK**L**QG (SEQ ID NO: 4), and a CDR3 comprising the sequence GWEGFAY (SEQ ID NO: 5); and (b) a light chain immunoglobulin variable region segment comprising: a CDR1 comprising the sequence RASENVDKYGNSFMH (SEQ ID NO: 6), a CDR2 comprising the sequence RASELQW (SEQ ID NO: 7), and a CDR3 comprising the sequence QRSNEVPWT (SEQ ID NO: 8).

In another aspect, the present disclosure provides an antibody molecule capable of binding dengue virus, comprising: (a) a heavy chain immunoglobulin variable region segment comprising: a CDR1 comprising the sequence D**V**YMS (SEQ ID NO: 3), a CDR2 comprising the sequence RIDPENGDTKYDPK**L**QG (SEQ ID NO: 4) or RIDPENGDTKYDPKFQG (SEQ ID NO: 35), and a CDR3 comprising the sequence GWEGFAY (SEQ ID NO: 5); and (b) a light chain immunoglobulin variable region segment comprising: a CDR1 comprising the sequence RASENVDKYGNSFMH (SEQ ID NO: 6), a CDR2 comprising the sequence RASELQW (SEQ ID NO: 7), and a CDR3 comprising the sequence QRSNEVPWT (SEQ ID NO: 8).

In some embodiments, **V** of HCDR1 is unchanged; in some embodiments, **L** of HCDR2 is unchanged, and in some embodiments, both **V** of HCDR1 and **L** of HCDR2 are unchanged.

In certain embodiments, the antibody molecule comprises a VH FR1 having the sequence QVQLVQSGAEVKKPGASVKVSCKAGFNIK (SEQ ID NO: 11), or an amino acid sequence having no more than 1, 2, 3, 4, or 5 mutations relative to SEQ ID NO: 11.

In certain embodiments, the antibody molecule comprises a VH FR2 having the sequence WVRQAPGQGLEWMG (SEQ ID NO: 84), or an amino acid sequence having no more than 1, 2, 3, 4, or 5 mutations relative to SEQ ID NO: 84. In certain embodiments, the antibody molecule comprises a VH FR2 having the sequence WVRQAPEQGLEWMG (SEQ ID NO: 85), or an amino acid sequence having no more than 1, 2, 3, 4, or 5 mutations relative to SEQ ID NO: 85.

In certain embodiments, the present disclosure provides an antibody molecule capable of binding dengue virus, comprising:

(a) a heavy chain immunoglobulin variable region segment comprising:

a FW1 comprising a deletion of position 26 relative to SEQ ID NO: 33;

a CDR1 comprising the sequence D**T**YMS (SEQ ID NO: 14) (or a sequence that differs by no more than, 1, 2, or 3 amino acids therefrom, optionally provided that **T** is unchanged), or a CDR1 comprising the sequence D**V**YMS (SEQ ID NO: 3) (or a sequence that differs by no more than, 1, 2, or 3 amino acids therefrom, optionally provided that **V** is unchanged),

a CDR2 comprising the sequence RIDPENGDTKYDPK**L**QG (SEQ ID NO: 4) (or a sequence that differs by no more than, 1, 2, 3, 4, or 5 amino acids therefrom, optionally provided that **L** is unchanged), and

a CDR3 comprising the sequence GWEGFAY (SEQ ID NO: 5) (or a sequence that differs by no more than, 1, 2, or 3 amino acids therefrom); and

(b) a light chain variable region segment comprising:

a CDR1 comprising the sequence RASENVDKYGNSFMH (SEQ ID NO: 6) (or a sequence that differs by no more than, 1, 2, 3, 4, or 5 amino acids therefrom),

a CDR2 comprising the sequence RASELQW (SEQ ID NO: 7) (or a sequence that differs by no more than, 1, 2, or 3 amino acids therefrom), and

a CDR3 comprising the sequence QRSNEVPWT (SEQ ID NO: 8) (or a sequence that differs by no more than, 1, 2, or 3 amino acids therefrom).

In an aspect, the present disclosure provides an antibody molecule capable of binding dengue virus, comprising: (a) a heavy chain immunoglobulin variable region segment comprising: a FR1 comprising a deletion of position 26 according to the VH amino acid sequence of SEQ ID NO: 33; a CDR1 comprising the sequence D**V**YMS (SEQ ID NO: 3) or DTYMS (SEQ ID NO: 14), a CDR2 comprising the sequence RIDPENGDTKYDPK**L**QG (SEQ ID NO: 4) or RIDPENGDTKYDPKFQG (SEQ ID NO: 35), and a CDR3 comprising the sequence GWEGFAY (SEQ ID NO: 5); and (b) a light chain immunoglobulin variable region segment comprising: a CDR1 comprising the sequence RASENVDKYGNSFMH (SEQ ID NO: 6), a

CDR2 comprising the sequence RASELQW (SEQ ID NO: 7), and a CDR3 comprising the sequence QRSNEVPWT (SEQ ID NO: 8).

In certain embodiments, the antibody molecule comprises a VH FR2 having the sequence WVRQAPGQGLEWMG (SEQ ID NO: 84), or an amino acid sequence having no more than 1, 2, 3, 4, or 5 mutations relative to SEQ ID NO: 84. In certain embodiments, the antibody molecule comprises a VH FR2 having the sequence WVRQAPEQGLEWMG (SEQ ID NO: 85), or an amino acid sequence having no more than 1, 2, 3, 4, or 5 mutations relative to SEQ ID NO: 85.

In certain embodiments, the present disclosure provides an antibody molecule, optionally capable of binding dengue virus, comprising:

(a) a heavy chain immunoglobulin variable region segment comprising:

a CDR1 comprising the sequence D**V**YMS (SEQ ID NO: 3) (or a sequence that differs by no more than, 1, 2, or 3 amino acids therefrom, optionally provided that **V** is unchanged),

a CDR2 comprising the sequence RIDPENGDTKYDPK**L**QG (SEQ ID NO: 4) (or a sequence that differs by no more than, 1, 2, 3, 4, or 5 amino acids therefrom, optionally provided that **L** is unchanged), and

excipient, or stabilizer, optionally admixed with the antibody molecule. The kit may also comprise a delivery device, *e.g.*, one comprising a syringe or needle. The kit may also comprise instructions for use.

In certain embodiments, the present disclosure provides a method of neutralizing dengue virus, comprising: contacting the dengue virus with an antibody molecule as described herein. In another aspect, the present disclosure provides a use of an antibody molecule as disclosed herein in the manufacture of a medicament for neutralizing dengue virus. In some embodiments, the dengue virus is of serotype DV-1, DV-2, DV-3, or DV-4.

In some embodiments, the present disclosure provides a method of treating a dengue virus infection, comprising administering to a subject in need thereof an isolated antibody molecule as described herein, in an amount effective to treat the virus. The method may further comprise administering an anti-viral agent to the subject, *e.g.*, an anti-viral agent chosen from one or more of balapiravir, chloroquine, celgosivir, ivermectin, or Carica folia. In certain embodiments, the antiviral agent is a second anti-dengue antibody molecule, *e.g.*, an anti-dengue antibody molecule described herein different from a first anti-dengue antibody molecule. In other embodiments, the antiviral agent is selected from an alpha-glucosidase I inhibitor (*e.g.*, celgosivir), an adenosine nucleoside inhibitor (*e.g.*, NITD008); an RNA-dependent RNA polymerase (RdRp) inhibitor (*e.g.*, NITD107), an inhibitor of host pyrimidine biosynthesis, *e.g.*, host dihydroorotate dehydrogenase (DHODH) (*e.g.*, NITD-982 and brequinar), an inhibitor of viral NS4B protein (*e.g.*, NITD-618), and an iminosugar (*e.g.*, UV-4). The method may further comprise administering a vaccine to the subject, *e.g.*, a dengue virus vaccine. In some embodiments, administration of the antibody molecule is parenteral or intravenous. In an aspect, the present disclosure provides the use of an isolated antibody molecule as described herein, or a pharmaceutical composition as described herein, in the manufacture of a medicament for treating dengue virus in a subject.

The disclosure also provides prophylactic methods. In some embodiments, a method of preventing a dengue virus infection by administering an antibody molecule as disclosed herein to a subject who is not, at the time, infected with dengue virus. For instance, in certain embodiments, the present disclosure provides a method of reducing a patient's risk of contracting dengue virus, comprising administering to a subject in need thereof an isolated antibody molecule as described herein, in an amount effective to reduce the risk of contracting the virus. For example the risk of contracting dengue virus may be reduced by, *e.g.*, at least 25%, 50%, 75%, 80%, 85%, 90%, 95%, 97%, 98%, 99%, or more. In some embodiments, the antibody molecule is provided to a patient who is not infected with dengue virus, with the result that if infection occurs, the course of the disease is likely to be milder than the course of disease in a similar patient who has not

uninfected subject (*e.g.*, human) can be further reduced, *e.g.*, at least about 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, or 90%.

In certain embodiments, this disclosure provides a method of detecting dengue virus in a biological sample, comprising (i) contacting the sample or the subject (and optionally, a reference sample or subject) with an antibody molecule described herein under conditions that allow interaction of the antibody molecule and the polypeptide to occur, and (ii) detecting formation of a complex between the antibody molecule and the sample or the subject (and optionally, the reference sample or subject). In one aspect, the present disclosure provides a method of detecting dengue virus in a biological sample, comprising (i) contacting the biological sample with an antibody molecule as disclosed herein under conditions that allow interaction of the antibody molecule and the polypeptide to occur, and (ii) detecting formation of a complex between the antibody molecule and the biological sample.

In some embodiments, this disclosure provides an anti-dengue antibody molecule comprising a VH region that has a deletion of position 26 relative to the VH of antibody A11. For instance,

We claim:

1. An antibody molecule capable of binding dengue virus, comprising:

(a) a heavy chain immunoglobulin variable region segment comprising:

a CDR1 comprising the sequence D**V**YMS (SEQ ID NO: 3) or DTYMS (SEQ ID NO: 14),

a CDR2 comprising the sequence RIDPENGDTKYDPK**L**QG (SEQ ID NO: 4), and

a CDR3 comprising the sequence GWEGFAY (SEQ ID NO: 5); and

(b) a light chain immunoglobulin variable region segment comprising:

a CDR1 comprising the sequence RASENVDKYGNSFMH (SEQ ID NO: 6),

a CDR2 comprising the sequence RASELQW (SEQ ID NO: 7), and

a CDR3 comprising the sequence QRSNEVPWT (SEQ ID NO: 8).

2. An antibody molecule capable of binding dengue virus, comprising:

(a) a heavy chain immunoglobulin variable region segment comprising:

a CDR1 comprising the sequence D**V**YMS (SEQ ID NO: 3),

a CDR2 comprising the sequence RIDPENGDTKYDPK**L**QG (SEQ ID NO: 4) or RIDPENGDTKYDPKFQG (SEQ ID NO: 35), and

a CDR3 comprising the sequence GWEGFAY (SEQ ID NO: 5); and

(b) a light chain immunoglobulin variable region segment comprising:

a CDR1 comprising the sequence RASENVDKYGNSFMH (SEQ ID NO: 6),

a CDR2 comprising the sequence RASELQW (SEQ ID NO: 7), and

a CDR3 comprising the sequence QRSNEVPWT (SEQ ID NO: 8).

3. The antibody molecule of claim 1 or 2, which comprises a VH FR1 having the sequence QVQLVQSGAEVKKPGASVKVSCKAGFNIK (SEQ ID NO: 11), or an amino acid sequence having no more than 1, 2, 3, 4, or 5 mutations relative to SEQ ID NO: 11, or a VH FR1 comprising a deletion of position 26 relative to SEQ ID NO: 33.

4. An antibody molecule capable of binding dengue virus, comprising:

(a) a heavy chain immunoglobulin variable region segment comprising:

a FR1 comprising a deletion of position 26 according to the VH amino acid sequence of SEQ ID NO: 33;

a CDR1 comprising the sequence DVYMS (SEQ ID NO: 3) or DTYMS (SEQ ID NO: 14),

a CDR2 comprising the sequence RIDPENGDTKYDPKLQG (SEQ ID NO: 4) or RIDPENGDTKYDPKFQG (SEQ ID NO: 35), and

a CDR3 comprising the sequence GWEGFAY (SEQ ID NO: 5); and

(b) a light chain immunoglobulin variable region segment comprising:

a CDR1 comprising the sequence RASENVDKYGNSFMH (SEQ ID NO: 6),

a CDR2 comprising the sequence RASELQW (SEQ ID NO: 7), and

a CDR3 comprising the sequence QRSNEVPWT (SEQ ID NO: 8).

5. The antibody molecule of any one of claims 1-4, which comprises a VH FR2 having the sequence WVRQAPGQGLEWMG (SEQ ID NO: 84) or WVRQAPEQGLEWMG (SEQ ID NO: 85), or an amino acid sequence having no more than 1, 2, 3, 4, or 5 mutations relative to SEQ ID NO: 84 or 85.

6. The antibody molecule of any of claims 1-5, which is capable of binding to dengue virus EDIII (E protein domain III).

7. The antibody molecule of any of claims 1-6, which comprises a VH CDR1 comprising the sequence of SEQ ID NO: 3, a VH CDR2 of SEQ ID NO: 4, a VH CDR3 of SEQ ID NO: 5, a VL CDR1 of SEQ ID NO: 6, a VL CDR2 of SEQ ID NO: 7, and a VL CDR3 of SEQ ID NO: 8.

8. The antibody molecule of any of claims 1-7, which comprises a VH amino acid sequence at least 70% identical to SEQ ID NO: 1.

9. The antibody molecule of any of claims 1-8, which comprises the VH amino acid sequence of SEQ ID NO: 1.

10. The antibody molecule of any of claims 1-9, which comprises a VH amino acid sequence at least 70% identical to any of SEQ ID NOS: 16-21, 25, 27, 29, 31, 32, 33, 36,

80, or 81, or the VH amino acid sequence of any of SEQ ID NOS: 16-21, 25, 27, 29, 31, 32, 33, 36, 80, or 81.

11. The antibody molecule of any of claims 1-10, which comprises a VL amino acid sequence at least 70% identical to SEQ ID NO: 2.

12. The antibody molecule of any of claims 1-11, which comprises the VL amino acid sequence of SEQ ID NO: 2.

13. The antibody molecule of any of claims 1-12, which comprises the VH amino acid sequence of SEQ ID NO: 1 and the VL amino acid sequence of SEQ ID NO: 2.

14. The antibody molecule of any of claims 1-10, which comprises a VL amino acid sequence at least 70% identical to SEQ ID NO: 34 or the VL amino acid sequence of SEQ ID NO: 34.

15. The antibody molecule of any of claims 1-14, which is a Fab, F(ab')2, Fv, or a single chain Fv fragment (scFv).

16. The antibody molecule of any of claims 1-14, which comprises (a) a heavy chain constant region selected from IgG1, IgG2, IgG3, and IgG4, (b) a light chain constant region chosen from the light chain constant regions of kappa or lambda, or both (a) and (b).

17. The antibody molecule of any of claims 1-16, which is an isolated antibody molecule or a humanized antibody molecule, or comprises one or more framework regions derived from a human framework germline sequence.

18. The antibody molecule of any of claims 1-17, which is capable of one, two, three, four, five, or all of the following:

(a) binding to dengue virus EDIII with a dissociation constant (K_D) of less than about 80, 70, 60, 50, 40, 30, 20, 10, 8, 6, 4, 3, 2, 1, 0.5, 0.2, 0.1, 0.05, or 0.01 nM;

(b) binding to dengue virus serotype DV-4 EDIII with a dissociation constant (KD) of less than about 10, 8, 6, 5, 4, or 3 nM;

(c) binding to DV-3 or DV-4 EDIII domain with at least a 2, 3, 4, 5, 6, 8, 10, 12, 15, 25, 50, 75, 100, 1,000, 5,000, or 10,000-fold greater affinity than antibody A11 or antibody 4E11;

(d) binding to a dengue virus strain selected from DENV-4 BC2, DENV-4-Sing, DENV-4 NC, DENV-4 Phil, DENV-3 Sing, DENV-3 Nic, DENV-3 H87, DENV-2 Peru, DENV-2 Sing, DENV-2 NGC, DENV-1 Hawaii/1944, DENV-2 New Guinea/1944 (NGC), DENV-3 Philippines/1956 (H87), DENV-4 Mexico/1997 (BC287/97), and DENV-4 H241, with at least 2, 3, 4, 5, 6, 8, 10, 12, 25, 50, 75, 100, or 1,000-fold greater affinity than antibody A11 or antibody 4E11;

(e) neutralizing dengue virus in a focus reduction neutralization test; or

(f) neutralizing dengue virus with an IC50 that is at least 2, 3, 4, 5, 6, 8, 10, 12, 25, 50, 75, or 100-fold lower than antibody A11 or antibody 4E11 in a focus reduction neutralization test.

19. A pharmaceutical composition comprising the antibody molecule of any of claims 1-18 and a pharmaceutically acceptable carrier, excipient, or stabilizer.

20. A nucleic acid encoding the antibody heavy or light chain variable region of the antibody molecule of any of claims 1-18.

21. An expression vector comprising the nucleic acid of claim 20.

22. A host cell comprising the nucleic acid of claim 20.

23. A method of producing an antibody molecule or fragment thereof, comprising culturing the host cell of claim 22 under conditions suitable for gene expression.

24. A kit comprising a container having disposed therein an antibody molecule of any of claims 1-18; a pharmaceutically acceptable carrier, excipient, or stabilizer; and optionally a delivery device, optionally wherein the delivery device comprises a syringe or needle, and optionally wherein the kit further comprises instructions for use.

25. Use of an antibody molecule of any of claims 1-18 in the manufacture of a medicament for neutralizing dengue virus.

26. The use of claim 25, wherein the dengue virus is of serotype DV-1, DV-2, DV-3, or DV-4.

27. Use of an isolated antibody molecule of any of claims 1-18, or a pharmaceutical composition of claim 19, in the manufacture of a medicament for treating dengue virus in a subject.

28. The use of claim 27, wherein the antibody molecule or pharmaceutical composition is to be used in combination with an anti-viral agent or vaccine.

29. The use of claim 27, wherein the anti-viral agent is:

(a) chosen from one or more of balapiravir, chloroquine, celgosivir, ivermectin, or Carica folia;

(b) an anti-dengue antibody different from the antibody molecule of any of claims 1-16;

(c) an anti-dengue antibody chosen from one or more of any of the antibodies listed in Table 1, 4E11, 14c10, 1F4, 2D22, 5J7, DV1.1, DV1.6, DV3.7, DV4.4, DV5.1, DV6.1, DV7.5, DV8.1, DV10.16, DV13.4, DV13.8, DV14.5, DV14.5, DV15.7, DV16.5, DV16.8, DV17.6, DV18.21, DV18.4, DV19.3, DV20.1, DV21.1, DV21.5, DV22.3, DV22.3 LALA, DV23.13, DV25.5, DV27.2, DV28.1, DV28.8, DV34.4, DV35.3, DV38.1, DV51.6, DV52.1, DV53.4, DV54.7, DV55.1, DV56.12, DV54.7, DV57.4, DV59.3, DV60.3, DV61.2, DV62.5, DV63.1, DV64.3, DV65.5, DV66.1, DV67.9, DV68.2, DV69.6, DV70.1, DV71.1, DV74.4, DV75.9, DV76.5, DV77.5, DV78.6, DV79.3, DV82.11, DV82.11 LALA, DV86.2, DV87.1, DV87.1 LALA, DV90.3, DV257.13, DV291.7, DV415.8, DV470.12, 3-147, 58/5, 2F5, 2G4, 5F9, 135.3, 2H12, 1A5, or 1C19; or

(d) chosen from one or more of an alpha-glucosidase I inhibitor, an adenosine nucleoside inhibitor, an inhibitor of NS3 and/or its cofactor NS2B, an RNA-dependent RNA polymerase (RdRp) inhibitor, an inhibitor of host pyrimidine biosynthesis, an inhibitor of viral NS4B protein, or an iminosugar.

30. The use of claim 29, wherein the alpha-glucosidase I inhibitor is celgosivir, the adenosine nucleoside inhibitor is NITD008, the inhibitor of NS3 and/or its cofactor NS2B is a [5-amino-1-(phenyl)sulfonyl-pyrazol-3-yl] compound, the RNA-dependent RNA

polymerase (RdRp) inhibitor is NITD107, the inhibitor of host pyrimidine biosynthesis is an inhibitor of host dihydroorotate dehydrogenase (DHODH) selected from NITD-982 or brequinar, the inhibitor of viral NS4B protein is NITD-618, or the iminosugar is UV-4.

31. The use of any of claims 28-30, wherein the antibody molecule or pharmaceutical composition is to be administered parenterally or intravenously.

32. The use of any of claims 28-31, wherein the antibody molecule neutralizes one, two, three, or all of dengue virus serotypes DV-1, DV-2, DV-3, or DV-4.

33. The use of any of claims 28-32, wherein the subject is infected with dengue virus or is at risk of being infected with dengue virus.

34. The use of any of claims 28-33, wherein the antibody molecule or pharmaceutical composition is to be administered prior to the subject being exposed to dengue virus or prior to onset of one or more manifestation of dengue virus.

35. Use of an isolated antibody molecule of any of claims 1-18, or a pharmaceutical composition of claim 19, in the manufacture of a medicament for preventing dengue virus infection in a subject

36. Use of an isolated antibody molecule of any of claims 1-18, or a pharmaceutical composition of claim 19, in the manufacture of a medicament for reducing a patient's risk of contracting dengue virus.

37. Use of an isolated antibody molecule of any of claims 1-18, or a pharmaceutical composition of claim 19, in the manufacture of a medicament for reducing transmission of dengue virus between a subject and a mosquito.

38. A method of detecting dengue virus in a biological sample, comprising (i) contacting the biological sample with an antibody molecule of any of claims 1-18 under conditions that allow interaction of the antibody molecule and the polypeptide to occur, and (ii) detecting formation of a complex between the antibody molecule and the biological sample.

39. The method of claim 38, further comprising contacting a reference sample with the antibody molecule of any of claims 1-18 under conditions that allow interaction of the antibody molecule and the polypeptide to occur, and detecting formation of a complex between the antibody molecule and the reference sample.