What is claimed:

1. An engineered meganuclease that recognizes and cleaves a recognition sequence consisting of SEQ ID NO: 16, wherein said engineered meganuclease comprises a first subunit and a second subunit, wherein said first subunit binds to a first recognition half-site of said recognition sequence and comprises a first hypervariable (HVR1) region, and wherein said second subunit binds to a second recognition half-site of said recognition sequence and comprises a second hypervariable (HVR2) region, and wherein said engineered meganuclease comprises an amino acid sequence having at least 96% sequence identity to SEQ ID NO: 33.

2. The engineered meganuclease of claim 1, wherein said first subunit comprises an amino acid sequence having at least 96% sequence identity to residues 198-344 of SEQ ID NO: 33, and wherein said second subunit comprises an amino acid sequence having at least 96% sequence identity to residues 7-153 of SEQ ID NO: 33.

3. The engineered meganuclease of claim 1 or claim 2, wherein said first subunit comprises residues 198-344 of SEQ ID NO: 33.

4. The engineered meganuclease of any one of claims 1-3, wherein said second subunit comprises residues 7-153 of SEQ ID NO: 33.

5. The engineered meganuclease of any one of claims 1-4, wherein said engineered meganuclease comprises the amino acid sequence of SEQ ID NO: 33.

6. An engineered meganuclease that recognizes and cleaves a recognition sequence consisting of SEQ ID NO: 16, wherein said engineered meganuclease comprises a first subunit and a second subunit, wherein said first subunit binds to a first recognition half-site of said recognition sequence and comprises:

(a) an amino acid sequence having at least 95% sequence identity to residues 198-344 of any one of SEQ ID NOs: 33-39; and

(b) a first hypervariable (HVR1) region comprising an amino acid sequence having at least 95% sequence identity to residues 215-270 of any one of SEQ ID NOs: 33-39;

and wherein said second subunit binds to a second recognition half-site of said recognition sequence and comprises:

(i) an amino acid sequence having at least 95% sequence identity to residues 7-153 of any one of SEQ ID NOs: 33-39; and

(ii) a second hypervariable (HVR2) region comprising an amino acid sequence having at least 95% sequence identity to residues 24-79 of any one of SEQ ID NOs: 33-39.

7. The engineered meganuclease of claim 6, wherein said HVR1 region comprises residues corresponding to residues 215, 217, 219, 221, 223, 224, 229, 231, 233, 235, 237, 259, 261, 266, and 268 of any one of SEQ ID NOs: 33-39.

8. The engineered meganuclease of claim 6 or claim 7, wherein said HVR1 region comprises residues 215-270 of any one of SEQ ID NOs: 33-39.

9. The engineered meganuclease of any one of claims 6-8, wherein said HVR2 region comprises residues corresponding to residues 24, 26, 28, 30, 32, 33, 38, 40, 42, 44, 46, 68, 70, 75, and 77 of any one of SEQ ID NOs: 33-39.

10. The engineered meganuclease of any one of claims 6-9, wherein said HVR2 region comprises residues 24-79 of any one of SEQ ID NOs: 33-39.

11. The engineered meganuclease of any one of claims 6-10, wherein said first subunit comprises residues 198-344 of any one of SEQ ID NOs: 33-39.

12. The engineered meganuclease of any one of claims 6-11, wherein said second subunit comprises residues 7-153 of any one of SEQ ID NOs: 33-39.

13. The engineered meganuclease of any one of claims 6-12, wherein said engineered meganuclease comprises a linker, wherein said linker covalently joins said first subunit and said second subunit.

14. The engineered meganuclease of any one of claims 6-13, wherein said engineered meganuclease comprises the amino acid sequence of any one of SEQ ID NOs: 33-39.

15. An engineered meganuclease that recognizes and cleaves a recognition sequence consisting of SEQ ID NO: 12, wherein said engineered meganuclease comprises a first subunit and a second subunit, wherein said first subunit binds to a first recognition half-site of said recognition sequence and comprises:

(a) an amino acid sequence having at least 95% sequence identity to residues 198-344 of any one of SEQ ID NOs: 22-24 or residues 7-153 of any one of SEQ ID NOs: 25-28; and

(b) a first hypervariable (HVR1) region comprising an amino acid sequence having at least 95% sequence identity to residues 215-270 of any one of SEQ ID NOs: 22-24 or residues 24-79 of any one of SEQ ID NOs: 25-28;

and wherein said second subunit binds to a second recognition half-site of said recognition sequence and comprises:

(i) an amino acid sequence having at least 95% sequence identity to residues 7-153 of any one of SEQ ID NOs: 22-24 or residues 198-344 of any one of SEQ ID NOs: 25-28; and

(ii) a second hypervariable (HVR2) region comprising an amino acid sequence having at least 95% sequence identity to residues 24-79 of any one of SEQ ID NOs: 22-24 or residues 215-270 of any one of SEQ ID NOs: 25-28.

16. The engineered meganuclease of claim 15, wherein said HVR1 region comprises residues corresponding to residues 215, 217, 219, 221, 223, 224, 229, 231, 233, 235, 237, 259, 261, 266, and 268 of any one of SEQ ID NOs: 22-24, or residues corresponding to residues 24, 26, 28, 30, 32, 33, 38, 40, 42, 44, 46, 68, 70, 75, and 77 of any one of SEQ ID NOs: 25-28.

17. The engineered meganuclease of claim 15 or claim 16, wherein said HVR1 region comprises residues 215-270 of any one of SEQ ID NOs: 22-24 or residues 24-79 of any one of SEQ ID NOs: 25-28.

18. The engineered meganuclease of any one of claims 15-17, wherein said HVR2 region comprises residues corresponding to residues 24, 26, 28, 30, 32, 33, 38, 40, 42, 44, 46, 68, 70, 75, and 77 of any one of SEQ ID NOs: 22-24, or residues corresponding to residues 215, 217, 219, 221, 223, 224, 229, 231, 233, 235, 237, 259, 261, 266, and 268 of any one of SEQ ID NOs: 25-28.

19. The engineered meganuclease of any one of claims 15-18, wherein said HVR2 region comprises residues 24-79 of any one of SEQ ID NOs: 22-24 or residues 215-270 of any one of SEQ ID NOs: 25-28.

20. The engineered meganuclease of any one of claims 15-19, wherein said first subunit comprises residues 198-344 of any one of SEQ ID NOs: 22-24 or residues 7-153 of any one of SEQ ID NOs: 25-28.

21. The engineered meganuclease of any one of claims 15-20, wherein said second subunit comprises residues 7-153 of any one of SEQ ID NOs: 22-24 or residues 198-344 of any one of SEQ ID NOs: 25-28.

22. The engineered meganuclease of any one of claims 15-21, wherein said engineered meganuclease comprises a linker, wherein said linker covalently joins said first subunit and said second subunit.

23. The engineered meganuclease of any one of claims 15-22, wherein said engineered meganuclease comprises the amino acid sequence of any one of SEQ ID NOs: 22-28.

24. A polynucleotide comprising a nucleic acid sequence encoding said engineered meganuclease of any one of claims 1-23.

25. The polynucleotide of claim 24, wherein said polynucleotide is an mRNA.

26. A recombinant DNA construct comprising a nucleic acid sequence encoding said engineered meganuclease of any one of claims 1-23.

27. The recombinant DNA construct of claim 26, wherein said recombinant DNA construct encodes a viral vector comprising said nucleic acid sequence encoding said engineered meganuclease of any one of claims 1-23.

28. The recombinant DNA construct of claim 27, wherein said viral vector is a recombinant AAV vector.

29. A viral vector comprising a nucleic acid sequence encoding said engineered meganuclease of any one of claims 1-23.

30. The viral vector of claim 29, wherein said viral vector is a recombinant AAV vector.

31. A pharmaceutical composition for treatment of a subject having hepatitis B virus (HBV) or hepatocellular carcinoma caused by HBV, said pharmaceutical composition comprising a pharmaceutically acceptable carrier and:

(a) a nucleic acid encoding said engineered meganuclease of any one of claims 1-23; or

(b) said engineered meganuclease of any one of claims 1-23.

32. The pharmaceutical composition of claim 31, wherein said nucleic acid encoding said engineered meganuclease is an mRNA.

33. The pharmaceutical composition of claim 32, wherein said mRNA is encapsulated within lipid nanoparticles.

34. The pharmaceutical composition of claim 31, wherein said pharmaceutical composition comprises said viral vector of claim 29 or claim 30.

35. Use of:

(a) a nucleic acid encoding said engineered meganuclease of any one of claims 1-14, wherein said engineered meganuclease is expressed in a target cell in a subject in vivo; or

(b) said engineered meganuclease of any one of claims 1-14;

in the manufacture of a medicament for treating HBV,

wherein said engineered meganuclease has specificity for a recognition sequence consisting of SEQ ID NO: 16 in the genome of the Hepatitis B virus, and wherein said engineered meganuclease recognizes and cleaves said recognition sequence in said target cell, and wherein the infection and/or proliferation of HBV in said subject is reduced or eliminated.

36. Use of:

(a) a nucleic acid encoding said engineered meganuclease of any one of claims 15-23, wherein said engineered meganuclease is expressed in a target cell in a subject in vivo; or

(b) said engineered meganuclease of any one of claims 15-23;

in the manufacture of a medicament for treating HBV,

wherein said engineered meganuclease has specificity for a recognition sequence consisting of SEQ ID NO: 12 in the genome of the Hepatitis B virus, and wherein said engineered meganuclease recognizes and cleaves said recognition sequence in said target cell, and wherein the infection and/or proliferation of HBV in said subject is reduced or eliminated.

37. The use of claim 35 or claim 36, wherein said medicament comprises said pharmaceutical composition of any one of claims 31-34.

38. The use of any one of claims 35-37, wherein the medicament is formulated to deliver said engineered meganuclease, or said nucleic acid encoding said engineered meganuclease to a target hepatocyte cell.