What is Claimed is:

1. A composition comprising a guide RNA comprising:
    a) a guide sequence comprising the sequence of SEQ ID NO: 23;
    b) a guide sequence that is at least 17, 18, or 19 contiguous nucleotides of the sequence of SEQ ID NO: 23; or
    c) a guide sequence that is at least 85% identical to the sequence of SEQ ID NO: 23; or
    d) a guide sequence that is at least 85% complementary to a target sequence present in exon 2 of the human *TTR* gene at chromosomal coordinate chr18:31592987-31593007;

    wherein the guide RNA further comprises at least one modification comprising:

    phosphorothioate (PS) bonds between the first four nucleotides at the 5' end of the guide RNA and/or between the last four nucleotides at the 3' end of the guide RNA; and/or

    2'-O-methyl (2'-O-Me) modified nucleotides at the first three nucleotides at the 5' end of the guide RNA and/or the last three nucleotides at the 3' end of the guide RNA.

2. The composition of claim 1, wherein the guide sequence comprises a sequence that is at least 85% complementary to a target sequence present in exon 2 of the human TTR gene at chromosomal coordinate chr18:31592987-31593007.

3. The composition of claim 1 or claim 2, wherein the guide sequence comprises a sequence that is at least 90% complementary to the target sequence present in exon 2 of the human TTR gene at chromosomal coordinate chr18:31592987-31593007.

4. The composition of any one of claims 1-3, wherein the guide sequence comprises a sequence that is at least 95% complementary to the target sequence present in exon 2 of the human TTR gene at chromosomal coordinate chr18:31592987-31593007.

5. The composition of any one of claims 1-4, wherein the guide sequence comprises a sequence that is 100% complementary to the target sequence present in exon 2 of the human TTR gene at chromosomal coordinate chr18:31592987-31593007.

6. The composition of claim 1, wherein the guide sequence comprises a sequence that is at least 85% identical to the sequence of SEQ ID NO: 23.

7. The composition of claim 1 or claim 6, wherein the guide sequence comprises a sequence that is at least 90% identical to the sequence of SEQ ID NO: 23.

8. The composition of any one of claims 1 and 6-7, wherein the guide sequence comprises a sequence that is at least 95% identical to the sequence of SEQ ID NO: 23.

9. The composition of any of claim claims 1 and 6-8, wherein the guide sequence comprises SEQ ID NO: 23.

10. The composition of any one of claims 1-9, wherein the guide sequence is 20, 21, 22, 23, 24, or 25 nucleotides in length.

11. The composition of any one of claims 1-10, wherein the guide sequence is 20 nucleotides in length.

12. The composition of any one of claims 1 and 6-11, wherein the guide sequence consists of SEQ ID NO: 23.

13. The composition of any one of claims 1-12, wherein the guide RNA is a single guide RNA (sgRNA).

14. The composition of claim 13, wherein the sgRNA comprises, in 5' to 3' order (a) the guide sequence and (b) the sequence of SEQ ID NO: 125.

15. The composition of claim 13 or claim 14, wherein the sgRNA comprises a sequence that is at least 97% identical to the sequence of SEQ ID NO: 87.

16. The composition of any one of claims 13-15, wherein the sgRNA comprises the sequence of SEQ ID NO: 87.

17. The composition of any one of claims 13-16, wherein the at least one modification comprises:

i) phosphorothioate (PS) bonds between the first four nucleotides at the 5' end of the guide RNA and between the last four nucleotides at the 3' end of the guide RNA; and

ii) 2'-O-methyl (2'-O-Me) modified nucleotides at the first three nucleotides at the 5' end of the guide RNA and the last three nucleotides at the 3' end of the guide RNA.

18. The composition of any one of claims 1-12, wherein the guide RNA is a dual guide RNA (dgRNA) comprising a first RNA and a second RNA, the first RNA comprising a crRNA comprising the guide sequence, and the second RNA comprising a trRNA.

19. The composition of claim 18, wherein the crRNA comprises the nucleotides of SEQ ID NO: 126 following the guide sequence at its 3' end.

20. The composition of claim 18 or claim 19, wherein the crRNA consists of the guide sequence of SEQ ID NO: 23 followed by SEQ ID NO: 126 at the 3' end of the guide sequence, and the at least one modification comprises:

i) phosphorothioate (PS) bonds between the first four nucleotides at the 5' end of the guide RNA; and

ii) 2'-O-methyl (2'-O-Me) modified nucleotides at the first three nucleotides at the 5' end of the guide RNA.

21. The composition of any one of claims 1-20, wherein the guide RNA is associated with a lipid nanoparticle (LNP).

22. The composition of claim 21, wherein the LNP comprises a CCD lipid.

23. The composition of claim 22, wherein the CCD lipid is (9Z,12Z)-3-((4,4-bis(octyloxy)butanoyl)oxy)-2-((((3-(diethylamino)propoxy)carbonyl)oxy)methyl)propyloctadeca-9,12-dienoate (Lipid A) or an acetal analog thereof.

24. The composition of any one of claims 21-23, wherein the LNP further comprises a neutral lipid.

25. The composition of claim 24, wherein the neutral lipid is distearoylphosphatidylcholine (DSPC).

26. The composition of any one of claims 21-25, wherein the LNP further comprises a helper lipid.

27. The composition of claim 26, wherein the helper lipid is cholesterol.

28. The composition of any one of claims 21-27, wherein the LNP further comprises a stealth lipid.

29. The composition of claim 28, wherein the stealth lipid is 1,2-dimyristoyl-sn-glycero-3-phosphothanolamine-N-[methoxy(polyethylene glycol)-2000] (PEG2k-DMG).

30. The composition of claim 21, wherein the LNP comprises a CCD lipid, a neutral lipid, a helper lipid, and a stealth lipid.

31. The composition of claim 30, wherein the CCD lipid is (9Z,12Z)-3-((4,4-bis(octyloxy)butanoyl)oxy)-2-((((3-(diethylamino)propoxy)carbonyl)oxy)methyl)propyloctadeca-9,12-dienoate, the neutral lipid is distearoylphosphatidylcholine (DSPC), the helper lipid is cholesterol, and the stealth lipid is 1,2-dimyristoyl-sn-glycero-3-phosphothanolamine-N-[methoxy(polyethylene glycol)-2000] (PEG2k-DMG).

32. The composition of any one of claims 1-31, wherein the composition further comprises an RNA-guided DNA binding agent or an mRNA comprising an open reading frame (ORF) encoding an RNA-guided DNA binding agent.

33. The composition of claim 32, wherein the composition comprises the mRNA comprising an ORF encoding the RNA-guided DNA binding agent, wherein the mRNA encodes a Cas9 nuclease comprising the amino acid sequence of SEQ ID NO: 213.

34. The composition of claim 32 or claim 33, wherein the composition comprises the mRNA comprising an ORF encoding the RNA-guided DNA binding agent, wherein the mRNA encodes a Cas9 nuclease comprising the amino acid sequence of SEQ ID NO: 203.

35. The composition of any one of claims 1-17 and 21-33, wherein the composition comprises an sgRNA comprising the sequence of SEQ ID NO: 87; an LNP comprising (9Z,12Z)-3-((4,4-bis(octyloxy)butanoyl)oxy)-2-((((3-(diethylamino)propoxy)carbonyl)oxy)methyl)propyloctadeca-9,12-dienoate, distearoylphosphatidylcholine (DSPC), cholesterol, and 1,2-dimyristoyl-sn-glycero-3-phosphothanolamine-N-[methoxy(polyethylene glycol)-2000] (PEG2k-DMG); and an mRNA encoding a Cas9 nuclease comprising the amino acid sequence of SEQ ID NO: 213.

36. The composition of any one of claim 1-12 and 18-33, wherein the composition comprises a dgRNA comprising a crRNA and a trRNA, wherein the crRNA comprises, in 5' to 3' order, the guide sequence of SEQ ID NO: 23 and the sequence of SEQ ID NO: 126; an LNP comprising (9Z,12Z)-3-((4,4-bis(octyloxy)butanoyl)oxy)-2-((((3-(diethylamino)propoxy)carbonyl)oxy)methyl)propyloctadeca-9,12-dienoate, distearoylphosphatidylcholine (DSPC), cholesterol, and 1,2-dimyristoyl-sn-glycero-3-phosphothanolamine-N-[methoxy(polyethylene glycol)-2000] (PEG2k-DMG); and an mRNA encoding a Cas9 nuclease comprising the amino acid sequence of SEQ ID NO: 213.

37. Use of a composition in the manufacture of a medicament for treating amyloidosis associated with deposition of transthyretin (ATTR) in a human subject, wherein the composition comprises a guide RNA comprising:

a) a guide sequence comprising the sequence of SEQ ID NO: 23; or
b) a guide sequence that is at least 17, 18, or 19 contiguous nucleotides of the sequence of SEQ ID NO: 23; or
c) a guide sequence that is at least 85% identical to the sequence of SEQ ID NO: 23; or
d) a guide sequence that is at least 85% complementary to a target sequence present in exon 2 of the human *TTR* gene at chromosomal coordinate chr18:31592987-31593007,

wherein the guide RNA comprises one or more modified nucleosides or nucleotides.

38. The use of claim 37, wherein the one or more modified nucleosides or nucleotides comprises one or more of:

a) replacement of one or both of the non-linking phosphate oxygens and/or of one or more of the linking phosphate oxygens in the phosphodiester backbone linkage;
b) replacement of a constituent of the ribose sugar;
c) replacement of the phosphate moiety with dephospho linkers;
d) modification or replacement of a naturally occurring nucleobase, including with a non-canonical nucleobase;
e) replacement or modification of the ribose-phosphate backbone;
f) modification of the 3' end or 5' end of the oligonucleotide; and
g) modification or replacement of the sugar.

39. The use of claim 37 or claim 38, wherein the one or more modified nucleosides or nucleotides comprises a 2' O methyl (2'-O-Me) modified nucleotide.

40. The use of any one of claims 37-39, wherein the one or more modified nucleosides or nucleotides comprises a phosphorothioate (PS) bond between nucleotides.

41. The use of any one of claims 37-40, wherein the one or more modified nucleosides or nucleotides comprises a 2' fluoro (2'-F) modified nucleotide.

42. The use of any one of claims 37-41, wherein the one or more modified nucleosides or nucleotides comprises a modification at one or more of the first five nucleotides at the 5' end of the guide RNA and/or at one or more of the last five nucleotides at the 3' end of the guide RNA.

43. Use of the composition of any one of claims 1-36 in the manufacture of a medicament for treating amyloidosis associated with deposition of transthyretin (ATTR) in a human subject.

44. The use of any one of claims 37-43, wherein the ATTR is wild-type ATTR.

45. The use of any one of claims 37-43, wherein the human subject has hereditary or familial amyloid polyneuropathy and/or has only or predominantly nerve symptoms of ATTR.

46. The use of any one of claims 37-43, wherein the human subject has hereditary or familial amyloid cardiomyopathy and/or has only or predominantly cardiac symptoms of ATTR.

47. The use of any one of claims 37-43 and 45-46, wherein the human subject expresses TTR having a V30 mutation; the human subject expresses TTR having a T60 mutation; or the human subject expresses TTR having a V122 mutation.

48. The use of claim 47, wherein the V30 mutation is V30A, V30G, V30L, or V30M; the T60 mutation is T60A; or the V122 mutation is V122A, V122I, or V122(-).

49. The use of any one of claims 37-44, wherein the human subject expresses wild-type TTR.