What is claimed is:

1. A guide RNA comprising:
    a. a guide sequence comprising at least 95%, 90%, or 85% identical to a sequence selected from SEQ ID NOs: 15, 8, and 41;
    b. a guide sequence comprising at least 17, 18, 19, or 20 contiguous nucleotides of a sequence selected from SEQ ID NOs: 15, 8, and 41; or
    c. a guide sequence selected from SEQ ID NOs: 15, 8, and 41.

2. The guide RNA of claim 1, further comprising the nucleotide sequence of SEQ ID NO: 202.

3. The guide RNA of claim 1, wherein the guide RNA further comprises a nucleotide sequence selected from SEQ ID NO: 170, 171, 172, and 173 wherein the sequence of SEQ ID NO: 170, 171, 172, or 173 is 3' of the guide sequence.

4. The guide RNA of any one of claims 1-3, wherein the guide RNA further comprises a 3' tail.

5. The guide RNA of any one of claims 1-4, wherein the guide RNA comprises at least one modification.

6. The guide RNA of claim 5, wherein the modification comprises a 5' end modification.

7. The guide RNA of claim 5 or 6, wherein the modification comprises a 3' end modification.

8. The guide RNA of any one of claims 1-7, wherein the guide RNA comprises a modification in a hairpin region.

9. The guide RNA of any one of claims 1-8, wherein the modification comprises a 2'-O-methyl (2'-O-Me) modified nucleotide.

10. The guide RNA of any one of claims 1-9, wherein the modification comprises a phosphorothioate (PS) bond between nucleotides.

11. The guide RNA of any one of claims 1-10, wherein the modification comprises a 2'-fluor (2'F) modified nucleotide.

12. The guide RNA of any one of claims 1 or 3-11, further comprising the nucleotide sequence of SEQ ID NO: 171.

13. The guide RNA of claim 12, modified according to the pattern of nucleotide sequence of SEQ ID NO: 405.

14. The guide RNA of any one of claims 1 or 3-11, further comprising the nucleotide sequence of SEQ ID NO: 173.

15. The guide RNA of claim 14, modified according to the pattern of SEQ ID NO: 248-255 or 450.

16. The guide RNA of any one of claims 12-15, wherein the guide sequence is SEQ ID NO: 15.

17. The guide RNA of any one of claims 12-15, wherein the guide sequence is SEQ ID NO: 8.

18. The guide RNA of any one of claims 12-15, wherein the guide sequence is SEQ ID NO: 41.

19. The guide RNA of any one of claims 1 or 4-11, wherein the guide RNA is modified according to the pattern of SEQ ID NO: 300, wherein the N's are collectively the guide sequence of claim 1.

20. The guide RNA of claim 16, wherein each N in SEQ ID NO: 300 is any natural or non-natural nucleotide.

21. The guide RNA of claim 19, wherein the guide sequence is SEQ ID NO: 15 and the guide RNA is modified according to mG*mG*mA* UUGCGUAUGGGACACAA GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGU CCGUUAUCAmAmCmUmUmGmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAm GmUmCmGmGmUmGmCmU*mU*mU*mU, wherein "mA," "mC," "mU," or "mG" denote a nucleotide that has been modified with 2'-O-Me, a * denotes a phosphorothioate bond, and an N is a natural nucleotide.

22. The guide RNA of claim 19, wherein the guide sequence is SEQ ID NO: 8 and the guide RNA is modified according to mU*mA*mC*CCGGGAGUUGACUUUGG GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGU CCGUUAUCAmAmCmUmUmGmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAm GmUmCmGmGmUmGmCmU*mU*mU*mU, wherein "mA," "mC," "mU," or "mG" denote a nucleotide that has been modified with 2'-O-Me, a * denotes a phosphorothioate bond, and N is a natural nucleotide.

23. The guide RNA of claim 19, wherein the guide sequence is SEQ ID NO: 41 and the guide RNA is modified according to mU*mA*mU*UAUCAAAUCACAUUACC GUUUUAGAmGmCmUmAmGmAmAmAmUmAmGmCAAGUUAAAAUAAGGCUAGU CCGUUAUCAmAmCmUmUmGmAmAmAmAmAmGmUmGmGmCmAmCmCmGmAm GmUmCmGmGmUmGmCmU*mU*mU*mU, wherein "mA," "mC," "mU," or "mG" denote

a nucleotide that has been modified with 2'-O-Me, a * denotes a phosphorothioate bond, and N is a natural nucleotide.

24. A composition comprising a guide RNA of any one of claims 1-23.

25. A composition of claim 24, further comprising an RNA-guided DNA binding agent or nucleic acid encoding an RNA-guided DNA binding agent.

26. The composition of claim 25, wherein the nucleic acid encoding an RNA-guided DNA binding agent comprises an mRNA comprising an open reading frame (ORF) encoding an RNA guided DNA binding agent.

27. The composition of claim 25 or 26, wherein the RNA-guided DNA binding agent is Cas9.

28. The composition of claim 27, wherein the Cas9 is S. pyogenes Cas9.

29. The composition of any one of claims 26-28, wherein the ORF is a modified ORF.

30. The composition of any one of claims 24-29, further comprising a pharmaceutical excipient.

31. The composition of any one of claims 24-30, wherein the guide RNA is associated with a lipid nanoparticle (LNP).

32. The composition of claim 31, wherein the LNP comprises a cationic lipid.

33. The composition of claim 32, wherein the cationic lipid is (9Z,12Z)-3-((4,4-bis(octyloxy)butanoyl)oxy)-2-((((3-(diethylamino)propoxy)carbonyl)oxy)methyl)propyl octadeca-9,12-dienoate, also called 3-((4,4-bis(octyloxy)butanoyl)oxy)-2-((((3-(diethylamino)propoxy)carbonyl)oxy)methyl)propyl (9Z,12Z)-octadeca-9,12-dienoate.

34. The composition of any one of claims 31-33, wherein the LNP comprises (9Z,12Z)-3-((4,4-bis(octyloxy)butanoyl)oxy)-2-((((3-(diethylamino)propoxy)carbonyl)oxy)methyl)propyl octadeca-9,12-dienoate, also called 3-((4,4-bis(octyloxy)butanoyl)oxy)-2-((((3-(diethylamino)propoxy)carbonyl)oxy)methyl)propyl (9Z,12Z)-octadeca-9,12-dienoate, DSPC, cholesterol, and PEG2k-DMG.

35. A pharmaceutical composition comprising a guide RNA of any one of claims 1-23 or composition of any one of claims 24-34.

36. A pharmaceutical composition comprising or use of a guide RNA of any one of claims 1-23 or composition of any one of claims 24-34 for inducing a double stranded break or a single stranded break within a KLKB1 gene in a cell or reducing expression of KLKB1 in a cell.

37. The pharmaceutical composition or use of claim 36, for reducing expression of the KLKB1 gene in a cell or subject.

38. A pharmaceutical composition comprising or use of a guide RNA of any one of claims 1-23 or composition of any one of claims 24-34 for treating a subject having hereditary angioedema (HAE).

39. The pharmaceutical composition or use of claim 38, comprising reducing the frequency and/or severity of HAE attacks.

40. A pharmaceutical composition comprising or use of a guide RNA of any one of claims 1-23 or composition of any one of claims 24-34 for treating or preventing angioedema associated with HAE, bradykinin production and accumulation, bradykinin-induced swelling, angioedema obstruction of the airway, or asphyxiation.

41. A pharmaceutical composition or use of a guide RNA of any one of claims 1-23 or composition of any one of claims 24-34 for reducing total plasma kallikrein activity or reducing prekallikrein and/or kallikrein levels in a subject.

42. The pharmaceutical composition or use of claim 41, wherein the total plasma kallikrein activity is reduced by more than 60%.

43. A method or inducing a double stranded break or a single stranded break within a KLKB1 gene in a cell or reducing expression of KLKB1 in a cell comprising contacting a cell with a guide RNA of any one of claims 1-23 or composition of any one of claims 24-34.

44. The method of claim 43, wherein the cell is in a subject.

45. A method of treating a subject having hereditary angioedema (HAE) comprising administering a guide RNA of any one of claims 1-23 or composition of any one of claims 24-34 thereby treating the subject.

46. The method of claim 45, wherein treating the subject comprises reducing the frequency and/or severity of HAE attacks.

47. A method of treating or preventing angioedema associated with HAE, bradykinin production and accumulation, bradykinin-induced swelling, angioedema obstruction of the airway, or asphyxiation comprising administering to the subject a guide RNA of any one of claims 1-23 or composition of any one of claims 24-34, thereby treating or preventing angioedema associated with HAE, bradykinin production and accumulation, bradykinin-induced swelling, angioedema obstruction of the airway, or asphyxiation in the subject.

48. A method of reducing total plasma kallikrein activity in a subject comprising administrating a guide RNA of any one of claims 1-23 or composition of any one of claims 24-34, thereby reducing total plasma kallikrein activity in a subject.

49. The method of claim 48, wherein the total plasma kallikrein activity is reduced by more than 60% in the subject.

50. The use of a guide RNA of any one of claims 1-23 or composition of any one of claims 24-34 in the preparation of a medicament for practicing any of the methods of claims 43-49.