region, and a second linker region which connects the Cas9 region and the NLS region. In some embodiments, the GC% content of the TadA region is greater than 60%. In some embodiments, the GC% content of the TadA region is greater than or equal to 70%. In some embodiments, the GC% content of the Cas9 region is greater than 56%. In some embodiments, the GC% content of the Cas9 region is greater than or equal to 62%. In some embodiments, the GC% content of the NLS region is greater than 54%. In some embodiments, the GC% content of the NLS region is greater than or equal to 63%. In some embodiments, the GC% content of the first linker region is greater than 65%. In some embodiments, the GC% content of the first linker region is greater than or equal to 79%. In some embodiments, the GC% content of the second linker region is greater than 67%. In some embodiments, the GC% content of the second linker region is greater than or equal to 83%. In some embodiments, the GC% content of the TadA region is greater than 60%, the GC% content of the Cas9 region is greater than 56%, the GC% content of the NLS region is greater than 54%, the GC% content of the first linker region is greater than 65%, and the GC% content of the second linker region is greater than 67%. In some embodiments, the mRNA comprises a mRNA sequence selected from Table 23. In some embodiments, the mRNA comprises a mRNA sequence of SEQ ID No: 2136. In some embodiments, the mRNA comprises a poly A tail. In some embodiments, the composition further comprises a lipid nanoparticle (LNP) enclosing (i). In some embodiments, the LNP further encloses (ii). In some embodiments, the composition further comprises a second LNP enclosing (ii). In some embodiments, the ratio of the guide RNA and the mRNA encoding the base editor fusion protein is about 1:10 to about 10:1 by weight. In some embodiments, the ratio of the guide RNA and the mRNA encoding the base editor fusion protein is about 1:1, 1.5:1, 2:1, 3:1, 4:1, 1:1.5, 1:2, 1:3, or 1:4 by weight. In some embodiments, the ratio of the guide RNA and the mRNA encoding the base editor fusion protein is about 1:1 by weight.

[14a] In another aspect, provided herein is a composition for editing a gene target comprising: (i) an mRNA encoding a base editor protein comprising a DNA binding domain and a deaminase, wherein the mRNA comprises a sequence having at least 95% sequence identity to SEQ ID NO: 2192; and (ii) a guide RNA comprising a tracr sequence that serves as a binding scaffold for the base editor protein, and a spacer sequence that corresponds to a protospacer on a target gene, wherein the target gene is proprotein convertase subtilisin-kexin type 9 (PCSK9 gene).

[14b] In another aspect, there is provided a composition for editing a gene target

comprising: (i) an mRNA encoding a base editor protein comprising a DNA binding domain and a deaminase, wherein the mRNA comprises a sequence having at least 95% sequence identity to the coding sequence of SEQ ID NO: 2192, and (ii) a guide RNA comprising a tracr sequence that serves as a binding scaffold for the base editor protein, and a spacer sequence that corresponds to a protospacer on a target gene; wherein the target gene is proprotein convertase subtilisin-kexin type 9 (PCSK9).

[15] In another aspect, provided herein is a pharmaceutical composition comprising the composition as provided herein and a pharmaceutically acceptable carrier or excipient.

[15a] In another aspect, provided herein is a pharmaceutical composition, comprising the composition as described herein, for use in treatment or prevention of a condition in a subject in need thereof.

[16] In another aspect, provided herein is a method for treating or preventing a condition in a subject in need thereof, the method comprising administering to the subject a therapeutically effective amount of the composition as provided herein. In some embodiments, the administration is via intravenous infusion. In some embodiments, the method comprises sequential administration of a LNP enclosing (i) and a LNP enclosing (ii). In some embodiments, the method comprises concurrent administration of the t LNP enclosing (i) and the LNP enclosing (ii). In some embodiments, the method comprises

CLAIMS

1. A composition for editing a gene target comprising:

(i) an mRNA encoding a base editor protein comprising a DNA binding domain and a deaminase, wherein the mRNA comprises a sequence having at least 95% sequence identity to SEQ ID NO: 2192; and

(ii) a guide RNA comprising a tracr sequence that serves as a binding scaffold for the base editor protein, and a spacer sequence that corresponds to a protospacer on a target gene, wherein the target gene is proprotein convertase subtilisin-kexin type 9 (PCSK9).

2. A composition for editing a gene target comprising: (i) an mRNA encoding a base editor protein comprising a DNA binding domain and a deaminase, wherein the mRNA comprises a sequence having at least 95% sequence identity to the coding sequence of SEQ ID NO: 2192, and (ii) a guide RNA comprising a tracr sequence that serves as a binding scaffold for the base editor protein, and a spacer sequence that corresponds to a protospacer on a target gene; wherein the target gene is proprotein convertase subtilisin-kexin type 9 (PCSK9).

3. The composition of claim 1 or 2, wherein the mRNA comprises a sequence having at least 99% sequence identity to SEQ ID NO: 2192.

4. The composition of claim 1 or 2, wherein the mRNA comprises a 5′UTR having at least 95% identity to the sequence of TABLE-US-00061 (SEQ ID NO: 2138) AGGAAAu′AAGAGAGAAAAGAAGAGu′AAGAAGAAAu′Au′AAGAGCCACC.

5. The composition of claim 1 or 2, wherein mRNA comprises a 3′UTR having at least 95% identity to the sequence of TABLE-US-00062 (SEQ ID NO: 2147) GCGGCCGCu′u′AAu′u′AAGCu′GCCu′u′Cu′GCGGGGCu′u′GCCu′u′Cu′GGCCAu′GCCCu′u′Cu′u′Cu′Cu′CCCu′u′GCACCu′Gu′ACCu′Cu′u′GGu′Cu′u′u′GAAu′AAAGCCu′GAGu′AGGAAGu′Cu′AGA.

6. The composition of claim 1 or 2, wherein the mRNA encoding the base editor protein comprises a GC % content greater than 50%.

7. The composition of claim 1 or 2, wherein the base editor protein further comprises an adenine tRNA deaminase (TadA) region, a Cas9 nickase region and a nuclear localization sequence (NLS) region.

8. The composition of claim 7, wherein the GC % content of the mRNA encoding the TadA region of the base editor protein is greater than 60%.
9. The composition of claim 7, wherein the GC % content of the mRNA encoding the Cas9 nickase region of the base editor protein is greater than 56%.
10. The composition of claim 7, wherein the GC % content of the mRNA encoding the NLS region of the base editor protein is greater than 54%.
11. The composition of claim 1 or 2, wherein the mRNA that encodes a base editor protein is selected from the group consisting of MA004, MA040, MA041, and MA045.
12. The composition of claim 11, wherein the mRNA is MA004.
13. The composition of claims 1-2, wherein the ratio of the guide RNA and the mRNA encoding the base editor protein is from 1:10 to 10:1 by weight.
14. The composition of claim 1 or 2, wherein the guide RNA further comprises a chemical modification on one or more nucleotides.
15. The composition of claim 14, wherein the chemical modification is selected from the group consisting of 2′-O-methyl modifications, 2′-O-(2-methoxyethyl) modifications, 2′-fluoro modifications, phosphonothioate modifications, inverted abasic modifications, deoxyribonucleotides, bicylic ribose analog (e.g., locked nucleic acid (LNA), C ethylene-bridged nucleic acid (ENA), bridged nucleic acid (BNA), unlocked nucleic acid (UNA)), base or nucleobase modifications, internucleoside linkage modifications, ribonebularine, 2′-O-methylnebularine, and 2′-deoxynebularine.
16. The composition of claim 1 or 2, wherein the guide RNA directs the base editor protein to effect a nucleobase alteration in the PCSK9 gene.
17. The composition of claim 16, wherein the nucleobase alteration results in a frame shift, a premature stop codon, an insertion or deletion in a transcript encoded by the PCSK9 gene.
18. The composition of claim 16, wherein the nucleobase alteration results in an aberrant transcript encoded by the PCSK9 gene.
19. The composition of claim 16, wherein the nucleobase alteration is at a splice donor site of the PCSK9 gene.
20. The composition of claim 16, wherein the splice donor site is at 5′ end of PCSK9 intron 1 as referenced in SEQ ID NO: 5.

21. The composition of claim 16, wherein the nucleobase alteration is at a splice acceptor site of the PCSK9 gene.

22. The composition of claim 1 or 2, wherein the protospacer comprises a sequence having at least 80% sequence identity to the sequence of 5′-CCCGCACCTTGGCGCAGCGG-3′ (SEQ ID No: 13) or to the sequence of 5′-CCGCACCTTGGCGCAGCGG-3′ (SEQ ID No: 247).

23. The composition of claim 1 or 2, wherein the guide RNA comprises a spacer sequence having at least 80% sequence identity to a spacer sequence of the guide RNA of SEQ ID NO: 9.

24. The composition of claim 23, wherein the guide RNA comprises an RNA sequence having the sequence of SEQ ID NO: 9.