CLAIMS

1. A non-naturally occurring nuclease system comprising one or more vectors comprising:

a bidirectional promoter selected from the group consisting of 7sk, SRP-RPS29, SNAR-G-l-CGBl, SNAR-CGB2, RMRP-CCDC 107, tRNA(Lys)-ALOXE3, RNU6-9-MED16: tRNA (Gly)-DPP9, RNU6-2-THEM259, and SNORD13-C8orf41,

wherein

a) one side of the bidirectional promoter is operably linked to at least one nucleotide sequence encoding a nuclease system guide RNA (gRNA), wherein the gRNA hybridizes with a target sequence of a DNA molecule or RNA molecule in a cell; and

b) the other side of the bidirectional promoter is operably linked to a nucleotide sequence encoding a genome-targeted nuclease,

wherein the gRNA targets and hybridizes with the target sequence and the nuclease cleaves one or both strands of the DNA molecule or RNA molecule.

2. The system of claim 1, wherein the system is CRISPR.

3. The system of claim 1, wherein the system is packaged into a single adeno-associated virus (AAV) particle.

4. The system of claim 1, wherein the system inactivates one or more gene products.

5. The system of claim 1, wherein the nuclease system excises at least one gene mutation.

6. The system of claim 1, further comprising a donor template.

7. The system of claim 2, wherein the nucleotide sequence encoding the genome-targeted nuclease is mutated so that the encoded genome-targeted nuclease lacks the ability to cleave one or both strands of the target polynucleotide.

8. The system of claim 1, further comprising at least one Kozak sequence.

9. The system of claim 1, further comprising an RNA sequence that mediates cap-independent initiation of translation.

10. The system of claim 1, wherein the promoter is a 7sk promoter.

11. The system of claim 10, wherein the 7sk promoter comprises a nucleotide sequence having at least 95% identity to the nucleotide sequence set forth in SEQ ID NOs: 3-8.

12. The system of claim 11, wherein the 7sk promoter comprises a nucleotide sequence set forth in SEQ ID NOs: 3-8.

13. A non-naturally occurring nuclease system comprising a vector comprising:

a) an RPPH1-PARP2 bidirectional promoter derived from *ailuropoda melanoleuca, callithrix jacchus, canis familiaris, cavia porcellus, chlorocebus sabaeus, choloepus hoffinanni, dasypus novemcinctus, dipodomys ordii, equus caballus, erinaceus europaeus, felis catus, gorilla gorilla, ictidomys tridecemlineatus, loxodonta africana, macaca mulatta, mustela putorius furo, myotis lucifugus, nomascus leucogenys, ochotona princeps, oryctolagus cuniculus, otolemur garnettii, ovis aries, pan troglodytes, papio anubis, pongo abelii, procavia capensis, pteropus vampyrus, sus scrofa, tarsius syrichta, tupaia belangeri, tursiops truncatus,* or *vicugna pacos*, wherein the bidirectional promoter comprises:

a) control elements that provide for transcription in one direction of at least one nucleotide sequence encoding a nuclease system guide RNA (gRNA), wherein the gRNA hybridizes with a target sequence of a DNA molecule or RNA molecule in a cell; and

b) control elements that provide for transcription in the opposite direction of a nucleotide sequence encoding a genome-targeted nuclease,

wherein the gRNA targets and hybridizes with the target sequence and the nuclease cleaves one or both strands of the DNA molecule or RNA molecule.

14. The system of claim 13, wherein the system is CRISPR.

15. The system of claim 13, wherein the system is packaged into a single adeno-associated virus (AAV) particle.

16. The system of claim 13, wherein the system inactivates one or more gene products.

17. The system of claim 13, wherein the nuclease system excises at least one gene mutation.

18. The system of claim 13, further comprising a donor template.

19. The system of claim 13, wherein the nucleotide sequence encoding the genome-targeted nuclease is mutated so that the encoded genome-targeted nuclease lacks the ability to cleave one or both strands of the target polynucleotide.

20. The system of claim 13, further comprising at least one Kozak sequence.

21. The system of claim 13, further comprising an RNA sequence that mediates cap-independent initiation of translation.

22. The system of any preceding claim, wherein the genome-targeted nuclease is a Cas9 nickase derived from *S. aureus* (SaCas9 nickase).

23. Use of the non-naturally occurring nuclease system of claim 1 in the manufacture of a medicament for the treatment of a disease selected from the group consisting of retinal dystrophy, corneal dystrophy, microsatellite expansion diseases, and cancer in a subject in need thereof, wherein the disease results from disruption in a disease-associated gene.

24. The non-naturally occurring nuclease system of claim 1 for use in the treatment of a disease selected from the group consisting of retinal dystrophy, corneal dystrophy, microsatellite expansion diseases, and cancer in a subject in need thereof, wherein the disease results from disruption in a disease-associated gene.

25. Use of the non-naturally occurring nuclease system of claim 13 in the manufacture of a medicament for the treatment of a disease selected from the group consisting of retinal dystrophy, corneal dystrophy, microsatellite expansion diseases, and cancer in a subject in need thereof, wherein the disease results from disruption in a disease-associated gene.

26. The non-naturally occurring nuclease system of claim 13 for use in the treatment of a disease selected from the group consisting of retinal dystrophy, corneal dystrophy, microsatellite expansion diseases, and cancer in a subject in need thereof, wherein the disease results from disruption in a disease-associated gene.