CLAIMS

~~What is claimed is:~~

1. An adenosine deaminase acting on ribonucleic acid (RNA) (ADAR) recruiting molecule comprising a double-stranded RNA duplex, wherein the double-stranded RNA duplex comprises two ~~strands of~~ RNA strands ~~of an equal number of nucleotides~~hybridized to form a duplex, wherein:

(a) the~~which~~ two RNA strands are not connected to one another by means of a hairpin~~, wherein:~~;

(~~a~~b) each of the two RNA strands forming the duplex has a 5' terminal nucleotide that is complementary to a 3' terminal nucleotide of the other RNA strand, wherein the terminal nucleotide is the terminal nucleotide of the duplex~~the 5′ nucleotide of each RNA strand is complementary to the 3′ nucleotide of the other RNA strand~~;

(~~b~~c) at least one of the two RNA strands forming ~~of~~ the ~~double-stranded RNA~~ duplex comprises at least one nucleoside modification and/or at least one backbone modification; and

(~~c~~d) the double-stranded RNA duplex comprises at least one base pair mismatch, wherein the mismatch is not positioned at either terminal nucleotide base pair of the ~~double-stranded RNA~~ duplex.

2. The ADAR recruiting molecule of claim 1, further comprising a single-stranded guide nucleic acid, optionally wherein the single-stranded guide nucleic acid comprises at least one nucleoside modification and/or at least one backbone modification.

3. The ADAR recruiting molecule of claim 1 or claim 2, wherein the double-stranded RNA duplex and/or the single-stranded guide nucleic acid comprises at least one nucleoside modification and at least one backbone modification.

4. The ADAR recruiting molecule of any one of claims 1-3, wherein the at least one nucleoside modification of the double-stranded RNA duplex comprises a 2′-aminoethyl, a 2′-deoxy-2′-fluoro-β-d-arabinonucleic acid, a 2′-O-methyl, a 2′-O-methoxyethyl (2'O-MOE), or a 2′-fluoro modification.

5. The ADAR recruiting molecule of any one of claims 1-4, wherein the at least one backbone modification of the double-stranded RNA duplex and/or the single-stranded guide nucleic acid comprises a phosphorothioate modification.

6. The ADAR recruiting molecule of any one of claims 1-5, wherein the at least one backbone modification of the double-stranded RNA duplex is positioned within 1-5 nucleotides of the terminal nucleotide of the RNA strand on which it is located and/or wherein the at least one backbone modification of a single-stranded guide nucleic acid is positioned within 1-5 nucleotides of the terminal nucleotide of the single-stranded guide nucleic acid.

~~7. The ADAR recruiting molecule of any one of claims 1-6, wherein the at least one backbone modification of the double-stranded RNA duplex is positioned within 1-3 nucleotides of the terminal nucleotide of the RNA strand on which it is located.~~

~~8. The ADAR recruiting molecule of any one of claims 1-7, wherein the at least one backbone modification of the double-stranded RNA duplex is positioned within 1 nucleotide of the terminal nucleotide of the RNA strand on which it is located.~~

~~9~~7. The ADAR recruiting molecule of any one of claims 1-~~8~~6, wherein the double-stranded RNA duplex and/or the single stranded guide nucleic acid comprises more than one nucleoside modification.

~~10. The ADAR recruiting molecule of any one of claims 1-9, wherein the double-stranded RNA duplex comprises more than two nucleoside modifications.~~

~~11. The ADAR recruiting molecule of any one of claims 1-10, wherein more than 25% of the nucleosides in the double-stranded RNA duplex comprise a nucleoside modification.~~

~~12. The ADAR recruiting molecule of any one of claims 1-11, wherein more than 50% of the nucleosides in the double-stranded RNA duplex comprise a nucleoside modification.~~

~~13. The ADAR recruiting molecule of any one of claims 1-12, wherein more than 75% of the nucleosides in the double-stranded RNA duplex comprise a nucleoside modification.~~

~~14. The ADAR recruiting molecule of any one of claims 1-13, wherein the double-stranded RNA duplex comprises~~and/or more than one backbone modification.

~~15. The ADAR recruiting molecule of any one of claims 1-14, wherein the double-stranded RNA duplex comprises more than two backbone modifications.~~

~~16. The ADAR recruiting molecule of any one of claims 1-15, wherein the double-stranded RNA duplex comprises more than three backbone modifications.~~

~~17. The ADAR recruiting molecule of any one of claims 1-16, wherein more than 25% of the internucleoside linkages of the double-stranded RNA duplex comprise a modification.~~

~~18. The ADAR recruiting molecule of any one of claims 1-17, wherein more than 50% of the internucleoside linkages of the double-stranded RNA duplex comprise a modification.~~

~~19. The ADAR recruiting molecule of any one of claims 1-18, wherein more than 75% of the internucleoside linkages of the double-stranded RNA duplex comprise a modification.~~

~~20~~8. The ADAR recruiting molecule of any one of claims 1-~~19~~7, further comprising nucleotides attached to the 3′ end or 5′ end of at least one of the RNA strands of the double-stranded RNA duplex creating a 3′ or 5′ end overhang.

~~21~~9. The ADAR recruiting molecule of any one of claims 1-~~20~~8, further comprising an additional moiety.

~~22~~10. The ADAR recruiting molecule of any one of claims 1-~~21~~9, further comprising a linker.

~~23. The ADAR recruiting molecule of any one of claims 2-22, wherein the single-stranded guide nucleic acid is guide Ribonucleic Acid (gRNA).~~

~~24. The ADAR recruiting molecule of any one of claims 2-23, wherein the single-stranded guide nucleic acid comprises at least one nucleoside modification.~~

~~25. The ADAR recruiting molecule of any one of claims 2-23, wherein the single-stranded guide nucleic acid comprises at least one backbone modification.~~

~~26. The ADAR recruiting molecule of any one of claims 2-25, wherein the single-stranded guide nucleic acid comprises at least one nucleoside modification and at least one backbone modification.~~

~~27. The ADAR recruiting molecule of any one of claims 2-26, wherein the single-stranded guide nucleic acid comprises at least two nucleoside modifications.~~

~~28. The ADAR recruiting molecule of any one of claims 2-27, wherein the single-stranded guide nucleic acid comprises at least three nucleoside modifications.~~

~~29. The ADAR recruiting molecule of any one of claims 2-28, wherein more than 25% of the nucleosides of the single-stranded guide nucleic acid comprise a nucleoside modification.~~

~~30. The ADAR recruiting molecule of any one of claims 2-29, wherein more than 50% of the nucleosides in the single-stranded guide nucleic acid comprise a nucleoside modification.~~

~~31. The ADAR recruiting molecule of any one of claims 2-30, wherein more than 75% of the nucleosides in the single-stranded guide nucleic acid comprise a nucleoside modification.~~

~~32. The ADAR recruiting molecule of any one of claims 2-31, wherein the single-stranded guide nucleic acid comprises at least one backbone modification.~~

~~33. The ADAR recruiting molecule of any one of claims 2-32, wherein the single-stranded guide nucleic acid comprises at least two backbone modifications.~~

~~34. The ADAR recruiting molecule of any one of claims 2-33, wherein the single-stranded guide nucleic acid comprises at least three backbone modifications.~~

~~35. The ADAR recruiting molecule of any one of claims 2-34, wherein more than 25% of the internucleoside linkages in the single-stranded guide nucleic acid comprise a phosphate modification.~~

~~36. The ADAR recruiting molecule of any one of claims 2-35, wherein more than 50% of the internucleoside linkages in the single-stranded guide nucleic acid comprise a phosphate modification.~~

~~37. The ADAR recruiting molecule of any one of claims 2-36, wherein more than 75% of the internucleoside linkages in the single-stranded guide nucleic acid comprise a phosphate modification.~~

~~38. The ADAR recruiting molecule of any one of claims 2-37, wherein the single-stranded guide nucleic acid comprises sufficient complementarity to hybridize with a target sequence.~~

~~39~~11. The ADAR recruiting molecule of any one of claims 2-~~38~~10, wherein the single-stranded guide nucleic acid comprises three consecutive non-modified nucleotides.

~~40~~12. The ADAR recruiting molecule of claim ~~39~~11, wherein at least one of the three consecutive non-modified nucleotides pairs with a nucleotide adjacent to a target adenosine in the target sequence.

~~41~~13. The ADAR recruiting molecule of claim ~~40~~12, wherein the middle nucleotide of the three consecutive non-modified nucleotides is opposite the target adenosine.

~~42~~14. The ADAR recruiting molecule of ~~any one of claims 2-41~~claim 13, wherein a nucleotide opposite a target adenosine comprises:

(a) cytosine (C);

(b) a natural or modified nucleotide which does not base pair with adenosine (A); and/or

(c) a natural or modified nucleotide which base pairs with guanine (G) or inosine (I).

~~43. The ADAR recruiting molecule of any one of claims 1-42, wherein each RNA strand of the double-stranded RNA duplex is at least 10 nucleotides in length.~~

~~44~~15. The ADAR recruiting molecule of any one of claims 1-~~43~~14, wherein each RNA strand of the double-stranded RNA duplex and/or the single-stranded guide nucleic acid is fewer than or equal to 100 nucleotides in length.

~~45. The ADAR recruiting molecule of any one of claims 1-44, wherein each RNA strand of the double-stranded RNA duplex is about 5 to about 80 nucleotides in length.~~

~~46. The ADAR recruiting molecule of any one of claims 1-45, wherein each RNA strand of the double-stranded RNA duplex is about 5 to about 60 nucleotides in length.~~

~~47. The ADAR recruiting molecule of any one of claims 1-46, wherein each RNA strand of the double-stranded RNA duplex is about 5 to about 40 nucleotides in length.~~

~~48. The ADAR recruiting molecule of any one of claims 1-47, wherein each RNA strand of the double-stranded RNA duplex is about 5 to about 30 nucleotides in length.~~

~~49. The ADAR recruiting molecule of any one of claims 1-48, wherein each RNA strand of the double-stranded RNA duplex is about 10 to about 27 nucleotides in length.~~

~~50. The ADAR recruiting molecule of any one of claims 1-49, wherein each RNA strand of the double-stranded RNA duplex is about 15 to about 26 nucleotides in length.~~

~~51. The ADAR recruiting molecule of any one of claims 2-50, wherein the single-stranded guide nucleic acid is at least 5 nucleotides in length.~~

~~52. The ADAR recruiting molecule of any one of claims 2-51, wherein the single-stranded guide nucleic acid is fewer than or equal to 100 nucleotides in length.~~

~~53. The ADAR recruiting molecule of any one of claims 2-52, wherein the single-stranded guide nucleic acid is about 5 to about 80 nucleotides in length.~~

~~54. The ADAR recruiting molecule of any one of claims 2-53, wherein the single-stranded guide nucleic acid is about 5 to about 60 nucleotides in length.~~

~~55. The ADAR recruiting molecule of any one of claims 2-54, wherein the single-stranded guide nucleic acid is about 5 to about 40 nucleotides in length.~~

~~56. The ADAR recruiting molecule of any one of claims 2-55, wherein the single-stranded guide nucleic acid is about 5 to about 30 nucleotides in length.~~

~~57. The ADAR recruiting molecule of any one of claims 2-56, wherein the single-stranded guide nucleic acid is about 10 to about 27 nucleotides in length.~~

~~58. The ADAR recruiting molecule of any one of claims 2-57, wherein the single-stranded guide nucleic acid is about 15 to about 26 nucleotides in length.~~

~~59. The ADAR recruiting molecule of any one of claims 2-58, wherein the single-stranded guide nucleic acid comprises at least 25% complementarity with a target sequence.~~

~~60. The ADAR recruiting molecule of any one of claims 2-59, wherein the single-stranded guide nucleic acid comprises at least 50% complementarity with a target sequence.~~

~~61. The ADAR recruiting molecule of any one of claims 2-60, wherein the single-stranded guide nucleic acid comprises at least 75% complementarity with a target sequence.~~

62. The ADAR recruiting molecule of any one of claims 2-61, wherein the single-stranded guide nucleic acid comprises at least 90% complementarity with a target sequence.

63. The ADAR recruiting molecule of any one of claims 2-62, wherein the single-stranded guide nucleic acid comprises at least 95% complementarity with a target sequence.

64. An RNA targeting molecule comprising:

(a) a double-stranded RNA duplex, wherein the double-stranded RNA duplex comprises two strands of RNA of an equal number of nucleotides, which two RNA strands are not connected to one another by means of a hairpin, wherein the 5′ nucleotide of each RNA strand is complementary to the 3′ nucleotide of the other RNA strand, wherein the double-stranded RNA duplex comprises at least one base pair mismatch, wherein the mismatch is not positioned at either terminal nucleotide base pair of the double-stranded RNA duplex; and

(b) a single-stranded guide nucleic acid.

65. The RNA targeting molecule of claim 64, wherein the double-stranded RNA duplex comprises at least one nucleoside modification and/or at least one backbone modification.

66. The RNA targeting molecule of claim 64 or claim 65, wherein the double-stranded RNA duplex comprises at least one nucleoside modification and at least one backbone modification.

67. The RNA targeting molecule of any one of claims 64-66, wherein the at least one nucleoside modification comprises a 2′-aminoethyl, a 2′-deoxy-2′-fluoro-β-d-arabinonucleic acid, a 2′-O-methyl, a 2′-O-methoxyethyl (2'O-MOE), or a 2′-fluoro modification.

68. The RNA targeting molecule of any one of claims 64-67, wherein the at least one backbone modification comprises a phosphorothioate modification.

~~69. The RNA targeting molecule of any one of claims 64-68, wherein the at least one backbone modification of the double-stranded RNA duplex is positioned within 1-5 nucleotides of the terminal nucleotide of the RNA strand on which it is located.~~

~~70. The RNA targeting molecule of any one of claims 64-69, wherein the at least one backbone modification of the double-stranded RNA duplex is positioned within 1-3 nucleotides of the terminal nucleotide of the RNA strand on which it is located.~~

~~71. The RNA targeting molecule of any one of claims 64-70, wherein the at least one backbone modification of the double-stranded RNA duplex is positioned within 1 nucleotide of the terminal nucleotide of the RNA strand on which it is located.~~

~~72. The RNA targeting molecule of any one of claims 64-71, wherein the double-stranded RNA duplex comprises more than one nucleoside modification.~~

~~73. The RNA targeting molecule of any one of claims 64-72, wherein the double-stranded RNA duplex comprises more than two nucleoside modifications.~~

~~74. The RNA targeting molecule of any one of claims 64-73, wherein more than 25% of the nucleosides in the double-stranded RNA duplex comprise a nucleoside modification.~~

~~75. The RNA targeting molecule of any one of claims 64-74, wherein more than 50% of the nucleosides in the double-stranded RNA duplex comprise a nucleoside modification.~~

~~76. The RNA targeting molecule of any one of claims 64-75, wherein more than 75% of the nucleosides in the double-stranded RNA duplex comprise a nucleoside modification.~~

~~77. The RNA targeting molecule of any one of claims 64-76, wherein the double-stranded RNA duplex comprises more than one backbone modification.~~

~~78. The RNA targeting molecule of any one of claims 64-77, wherein the double-stranded RNA duplex comprises more than two backbone modifications.~~

~~79. The RNA targeting molecule of any one of claims 64-78, wherein the double-stranded RNA duplex comprises more than three backbone modifications.~~

~~80. The RNA targeting molecule of any one of claims 64-79, wherein more than 25% of the internucleoside linkages of the double-stranded RNA duplex comprise a modification.~~

~~81. The RNA targeting molecule of any one of claims 64-80, wherein more than 50% of the internucleoside linkages of the double-stranded RNA duplex comprise a modification.~~

~~82. The RNA targeting molecule of any one of claims 64-81, wherein more than 75% of the internucleoside linkages of the double-stranded RNA duplex comprise a modification.~~

~~83. The RNA targeting molecule of any one of claims 64-82, further comprising nucleotides attached to the 3′ end or 5′ end of at least one of the RNA strands of the double-stranded RNA duplex creating a 3′ and/or 5′ end overhang.~~

~~84. The RNA targeting molecule of any one of claims 64-83, further comprising an additional moiety.~~

~~85. The RNA targeting molecule of any one of claims 64-84, further comprising a linker.~~

~~86. The RNA targeting molecule of any one of claims 64-85, wherein the single-stranded guide nucleic acid is guide ribonucleic acid (gRNA).~~

~~87. The RNA targeting molecule of any one of claims 64-86, wherein the single-stranded guide nucleic acid comprises at least one nucleoside modification.~~

~~88. The RNA targeting molecule of any one of claims 64-87, wherein the single-stranded guide nucleic acid comprises at least one backbone modification.~~

~~89. The RNA targeting molecule of any one of claims 64-88, wherein the single-stranded guide nucleic acid comprises at least one nucleoside modification and at least one backbone modification.~~

~~90. The RNA targeting molecule of any one of claims 64-89, wherein the single-stranded guide nucleic acid comprises at least two nucleoside modifications.~~

~~91. The RNA targeting molecule of any one of claims 64-90, wherein the single-stranded guide nucleic acid comprises at least three nucleoside modifications.~~

~~92. The RNA targeting molecule of any one of claims 64-91, more than 25% of the nucleosides of the single-stranded guide nucleic acid comprise a nucleoside modification.~~

~~93. The RNA targeting molecule of any one of claims 64-92, wherein more than 50% of the nucleosides in the single-stranded guide nucleic acid comprise a nucleoside modification.~~

~~94. The RNA targeting molecule of any one of claims 64-93, wherein more than 75% of the nucleosides in the single-stranded guide nucleic acid comprise a nucleoside modification.~~

~~95. The RNA targeting molecule of any one of claims 64-94, wherein the single-stranded guide nucleic acid comprises at least one backbone modification.~~

~~96. The RNA targeting molecule of any one of claims 64-95, wherein the single-stranded guide nucleic acid comprises at least two backbone modifications.~~

~~97. The RNA targeting molecule of any one of claims 64-96, wherein the single-stranded guide nucleic acid comprises at least three backbone modifications.~~

~~98. The RNA targeting molecule of any one of claims 64-97, wherein more than 25% of the internucleoside linkages in the single-stranded guide nucleic acid comprise a phosphate modification.~~

~~99. The RNA targeting molecule of any one of claims 64-98, wherein more than 50% of the internucleoside linkages in the single-stranded guide nucleic acid comprise a phosphate modification.~~

~~100. The RNA targeting molecule of any one of claims 64-99, wherein more than 75% of the internucleoside linkages in the single-stranded guide nucleic acid comprise a phosphate modification.~~

~~101. The RNA targeting molecule of any one of claims 64-100, wherein the single-stranded guide nucleic acid comprises sufficient complementarity to hybridize with a target sequence.~~

~~102. The RNA targeting molecule of any one of claims 64-101, wherein the single-stranded guide nucleic acid comprises three consecutive non-modified nucleotides.~~

~~103. The RNA targeting molecule of claim 102, wherein at least one of the three consecutive non-modified nucleotides of the single-stranded guide nucleic acid is complementary to a nucleotide adjacent to a target adenosine in the target sequence.~~

~~104. The RNA targeting molecule of claim 102 or claim 103, wherein the middle nucleotide of the three consecutive non-modified nucleotides is opposite the target adenosine.~~

~~105. The RNA targeting molecule of any one of claims 64-104, wherein a nucleotide opposite a target adenosine comprises:~~

~~(a) cytosine (C);~~

~~(b) a natural or modified nucleotide which does not base pair with adenosine (A); and/or~~

~~(c) a natural or modified nucleotide which base pairs with guanine (G) or inosine (I).~~

~~106. The RNA targeting molecule of any one of claims 64-105, wherein each RNA strand of the double-stranded RNA duplex is at least 5 nucleotides in length.~~

~~107. The RNA targeting molecule of any one of claims 64-106, wherein each RNA strand of the double-stranded RNA duplex is fewer than or equal to 100 nucleotides in length.~~

~~108. The RNA targeting molecule of any one of claims 64-107, wherein each RNA strand of the double-stranded RNA duplex is about 5 to about 80 nucleotides in length.~~

~~109. The RNA targeting molecule of any one of claims 64-108, wherein each RNA strand of the double-stranded RNA duplex is about 5 to about 60 nucleotides in length.~~

~~110. The RNA targeting molecule of any one of claims 64-109, wherein each RNA strand of the double-stranded RNA duplex is about 5 to about 40 nucleotides in length.~~

~~111. The RNA targeting molecule of any one of claims 64-110, wherein each RNA strand of the double-stranded RNA duplex is about 5 to about 30 nucleotides in length.~~

~~112. The RNA targeting molecule of any one of claims 64-111, wherein each RNA strand of the double-stranded RNA duplex is about 10 to about 27 nucleotides in length.~~

~~113. The RNA targeting molecule of any one of claims 64-112, wherein each RNA strand of the double-stranded RNA duplex is about 15 to about 26 nucleotides in length.~~

~~114. The RNA targeting molecule of any one of claims 64-113, wherein the single-stranded guide nucleic acid is at least 5 nucleotides in length.~~

~~115. The RNA targeting molecule of any one of claims 64-114, wherein the single-stranded guide nucleic acid is fewer than or equal to 100 nucleotides in length.~~

~~116. The RNA targeting molecule of any one of claims 64-115, wherein the single-stranded guide nucleic acid is about 5 to about 80 nucleotides in length.~~

~~117. The RNA targeting molecule of any one of claims 64-116, wherein the single-stranded guide nucleic acid is about 5 to about 60 nucleotides in length.~~

~~118. The RNA targeting molecule of any one of claims 64-117, wherein the single-stranded guide nucleic acid is about 5 to about 40 nucleotides in length.~~

~~119. The RNA targeting molecule of any one of claims 64-118, wherein the single-stranded guide nucleic acid is about 5 to about 30 nucleotides in length.~~

~~120. The RNA targeting molecule of any one of claims 64-119 wherein the single-stranded guide nucleic acid is about 10 to about 27 nucleotides in length.~~

~~121. The RNA targeting molecule of any one of claims 64-120, wherein the single-stranded guide nucleic acid is about 15 to about 26 nucleotides in length.~~

~~122. The RNA targeting molecule of any one of claims 64-121, wherein the single-stranded guide nucleic acid comprises at least 25% complementarity with a target sequence.~~

~~123. The RNA targeting molecule of any one of claims 64-122, wherein the single-stranded guide nucleic acid comprises at least 50% complementarity with a target sequence.~~

~~124. The RNA targeting molecule of any one of claims 64-123, wherein the single-stranded guide nucleic acid comprises at least 75% complementarity with a target sequence.~~

~~125. The RNA targeting molecule of any one of claims 64-124, wherein the single-stranded guide nucleic acid comprises at least 90% complementarity with a target sequence.~~

~~126. The RNA targeting molecule of any one of claims 64-125, wherein the single-stranded guide nucleic acid comprises at least 95% complementarity with a target sequence.~~

~~127~~16. Use of the ADAR recruiting molecule of any one of claims 2-15 in the manufacture of a medicament for ~~A method of~~ deaminating a target nucleic acid in a subject, ~~comprising, administering an effective amount of~~wherein the ADAR recruiting molecule is to be administered to the subject~~of any one of claims 2-63, and/or the RNA targeting molecule of any one of claims 64-126~~, wherein the ADAR recruiting molecule ~~and/or the RNA targeting~~

~~molecule~~ comprises a single-stranded guide nucleic acid comprising a sequence which is sufficiently complementary to a target sequence to hybridize with the target sequence.

~~128~~17. The ~~method~~ use of claim ~~127~~16, wherein the target sequence comprises a target adenosine.

~~129~~18. Use of the ADAR recruiting molecule of any one of claims 2-15 in the manufacture of a medicament for ~~A method of~~ treating a subject, ~~comprising administering~~wherein the ADAR recruiting molecule is to be administered to the subject~~of any one of claims 2-63, and/or the RNA targeting molecule of any one of claims 64-126~~, wherein the ADAR recruiting molecule ~~and/or the RNA targeting molecule~~ comprises a single-stranded guide nucleic acid comprising a sequence which is sufficiently complementary to a target sequence to hybridize with the target sequence.

~~130~~19. The ~~method~~ use of claim ~~129~~18, wherein the target sequence comprises a target adenosine.

~~131~~20. The ~~method~~ use of claim ~~130~~19, wherein the target adenosine is related to a disease or disorder, wherein the deamination of the target adenosine treats the disease or disorder.

~~132. The method of claim 131, wherein the disease or disorder is selected from: Cystic fibrosis, Hurler Syndrome, alpha-1-antitrypsin (A1AT) deficiency, Parkinson's disease, Alzheimer's disease, albinism, Amyotrophic lateral sclerosis, Asthma, beta-thalassemia (β-thalassemia), Cadasil syndrome, Charcot-Marie-Tooth disease, Chronic Obstructive Pulmonary Disease (COPD), Distal Spinal Muscular Atrophy (DSMA), Duchenne/Becker muscular dystrophy, Dystrophic Epidermolysis bullosa, Epidermylosis bullosa, Fabry disease, Factor V Leiden associated disorders, Familial Adenomatous, Polyposis, Galactosemia, Gaucher's Disease, Glucose-6-phosphate dehydrogenase, Haemophilia, Hereditary Hematochromatosis, Hunter Syndrome, Huntington's disease, Inflammatory Bowel Disease (IBD), Inherited polyagglutination syndrome, Leber congenital amaurosis, Lesch-Nyhan syndrome, Lynch syndrome, Marfan syndrome, Mucopolysaccharidosis, Muscular Dystrophy, Myotonic dystrophy types I and II, neurofibromatosis, Niemann-Pick disease type~~

A, B, and C, NY-eso1-related cancer, Peutz-Jeghers Syndrome, Phenylketonuria, Pompe's disease, Primary Ciliary Disease, Prothrombin mutation related disorders, such as the Prothrombin G20210A mutation, Pulmonary Hypertension, Retinitis Pigmentosa, Sandhoff Disease, Severe Combined Immune Deficiency Syndrome (SCID), Sickle Cell Anemia, Spinal Muscular Atrophy, Stargardt's Disease, Tay-Sachs Disease, Usher syndrome, X-linked immunodeficiency, Sturge-Weber Syndrome, and cancer.

133. An RNA targeting molecule comprising:

(a) a double-stranded RNA duplex comprising two RNA strands;

(b) a single-stranded guide nucleic acid; and

(c) a linker;

wherein the double-stranded RNA duplex is connected to the single-stranded guide nucleic acid via the linker.

134. The RNA targeting molecule of claim 133, wherein the linker is connected to the 5′ terminal nucleotide of one of the two strands of the RNA duplex.

135. The RNA targeting molecule of claim 133, wherein the linker is connected to the 3′ terminal nucleotide of one of the two strands of the RNA duplex.

136. The RNA targeting molecule of claim 133, wherein the linker is connected to a nucleotide located between the 5′ terminal nucleotide and the 3′ terminal nucleotide of one of the two strands of the RNA duplex.

137. The RNA targeting molecule of claim 133, wherein the linker is connected to the 5′ nucleotide of the guide nucleic acid.

138. The RNA targeting molecule of claim 133, wherein the linker is connected to the 3′ nucleotide of the guide nucleic acid.

~~139. The RNA targeting molecule of claim 133, wherein the linker is connected to a nucleotide located between the 5′ terminal nucleotide and the 3′ terminal nucleotide of the guide nucleic acid.~~

~~140. The RNA targeting molecule of claim 133, wherein the linker is connected to a sugar of the 5′ terminal nucleotide, or a 3′ hydroxyl or sugar of the 3′ terminal nucleotide of one strand of the RNA duplex.~~

~~141. The RNA targeting molecule of claim 133, wherein the linker is connected to a sugar of the 5′ terminal nucleotide, or a 3′ hydroxyl or sugar of the 3′ terminal nucleotide of the guide nucleic acid.~~

~~142. The RNA targeting molecule of claim 133, wherein the linker is connected to an internucleoside linkage of one RNA strand of the RNA duplex.~~

~~143. The RNA targeting molecule of claim 133, wherein the linker is connected to an internucleoside linkage of the guide nucleic acid.~~

~~144. The RNA targeting molecule of claim 133, wherein the linker is connected to a nucleoside sugar of one RNA strand of the RNA duplex.~~

~~145. The RNA targeting molecule of claim 133, wherein the linker is connected to a nucleoside sugar of the guide nucleic acid.~~

~~146. The RNA targeting molecule of claim 133, wherein the linker connects the 3′ end of the guide nucleic acid to the 5′ end of one RNA strand of the RNA duplex.~~

~~147. The RNA targeting molecule of claim 133, wherein the linker connects the 5′ end of the guide nucleic acid to the 3′ end of one RNA strand of the RNA duplex.~~

~~148. The RNA targeting molecule of claim 133, wherein the linker connects the 3′ end of the guide nucleic acid to the 3′ end of one RNA strand of the RNA duplex.~~

~~149. The RNA targeting molecule of claim 133, wherein the linker connects the 5′ end of the guide nucleic acid to the 5′ end of one RNA strand of the RNA duplex.~~

~~150. The RNA targeting molecule of claim 133, wherein the linker connects the 3′ end of the guide nucleic acid to a nucleotide located between the 5′ terminal nucleotide and the 3′ terminal nucleotide of one RNA strand of the RNA duplex.~~

~~151. The RNA targeting molecule of claim 150, wherein the linker is connected to an internucleoside linkage or a nucleoside sugar of one RNA strand of the RNA duplex.~~

~~152. The RNA targeting molecule of claim 133, wherein the linker connects the 5′ end of the guide nucleic acid to a nucleotide located between the 5′ terminal nucleotide and the 3′ terminal nucleotide of one RNA strand of the RNA duplex.~~

~~153. The RNA targeting molecule of claim 152, wherein the linker is connected to an internucleoside linkage or a nucleoside sugar of one RNA strand of the RNA duplex.~~

~~154. The RNA targeting molecule of claim 133, wherein the linker connects the 3′ end of one RNA strand of the RNA duplex to a nucleotide located between the 5′ terminal nucleotide and the 3′ terminal nucleotide of the guide nucleic acid.~~

~~155. The RNA targeting molecule of claim 154, wherein the linker is connected to an internucleoside linkage or a nucleoside sugar of the guide nucleic acid.~~

~~156. The RNA targeting molecule of claim 133, wherein the linker connects the 5′ end of one RNA strand of the RNA duplex to a nucleotide located between the 5′ terminal nucleotide and the 3′ terminal nucleotide of the guide nucleic acid.~~

~~157. The RNA targeting molecule of claim 156, wherein the linker is connected to an internucleoside linkage or a nucleoside sugar of the guide nucleic acid.~~

158. The RNA targeting molecule of claim 133, or any other prior claim, wherein the linker is an unbranched linker.

159. The RNA targeting molecule of claim 133, or any other prior claim, wherein the linker is a branched linker.

160. The RNA targeting molecule of claim 133, or any other prior claim, wherein the linker is a non-covalent linker comprising a first binding partner covalently attached to one strand of the double-stranded RNA duplex, and a second binding partner covalently attached to the single-stranded guide nucleic acid, wherein the first and second binding partners form a non-covalent complex connecting the double-stranded RNA duplex to the single-stranded guide nucleic acid.

161. The RNA targeting molecule of claim 160, wherein the first binding partner is a receptor and the second binding partner is a ligand specific for the receptor.

162. The RNA targeting molecule of claim 160, wherein the second binding partner is a receptor and the first binding partner is a ligand specific for the receptor.

163. The RNA targeting molecule of claim 160, wherein the first binding partner is biotin and the second binding partner is streptavidin.

164. The RNA targeting molecule of claim 160, wherein the first binding partner is streptavidin and the second binding partner is biotin.

165. The RNA targeting molecule of claim 133, or any other prior claim, wherein the linker is a covalent linker.

166. The RNA targeting molecule of claim 133, or any other prior claim, wherein the linker is greater than or equal to 4 atoms in length.

~~167. The RNA targeting molecule of claim 133, or any other prior claim, wherein the linker is fewer than or equal to 180 atoms in length.~~

~~168. The RNA targeting molecule of claim 165, wherein the linker comprises an alkyl, alkenyl, alkynyl, substituted alkyl, substituted alkenyl, substituted alkynyl, repeated ethylene glycol group, ether, thioether, urea, carbonate, amine, amide, maleimide-thioether, disulfide, phosphodiester, sulfonamide linkage, a product of a click reaction, a triazole from an azide-alkyne cycloaddition, carbamate, a cleavable linker, a redox cleavable linker, a reductively cleavable linker, a disulfide group, an acid cleavable linker, a hydrazone group, an ester group, an acetal group, a ketal group, an esterase cleavable linker, an ester group, a phosphatase cleavable linker, a phosphate group, a peptidase cleavable linker, a peptide bond, a bio-cleavable linker, DNA, RNA, disulfide, amide, functionalized monosaccharides, or oligosaccharides of galactosamine.~~

~~169. The RNA targeting molecule of claim 165, wherein the linker comprises a moiety derived from a click chemistry reaction.~~

~~170. The RNA targeting molecule of claim 169, wherein the moiety derived from a click chemistry reaction is a triazole, diazole, diazine, sulfide bond, maleimide ring, succinimide ring, ester, or amide.~~

~~171. The RNA targeting molecule of claim 165, wherein the linker comprises one or more amino acids.~~

~~172. The RNA targeting molecule of claim 165, wherein the linker comprises an organic molecule, group, polymer, or chemical domain.~~

~~173. The RNA targeting molecule of claim 172, wherein the chemical domain comprises an amide, urea, carbamate, carbonate, ester, acetal, ketal, phosphoramidite, hydrazone, imine, oxime, disulfide, silyl, hydrazine, hydrazone, thiol, imidazole, carbon-carbon bond, carbon-heteroatom bond, or azo domain.~~

~~174. The RNA targeting molecule of claim 165, wherein the linker is polymeric.~~

~~175. The RNA targeting molecule of claim 174, wherein the polymeric linker comprises polyethylene, polyethylene glycol, polyamide, polyester, or polyether.~~

~~176. The RNA targeting molecule of claim 133, or any other prior claim, wherein the linker comprises any one of Formula (I) – Formula (VII).~~

~~177. The RNA targeting molecule of claim 133, or any other prior claim, wherein the double-stranded RNA duplex comprises:~~

~~(a) an RNA strand comprising a sequence with at least 70% identity to Strand Ref.: 24 or 27; and~~

~~(b) an RNA strand comprising a sequence with at least 70% identity to Strand Ref.: 25 or 28;~~

~~and wherein the single-stranded guide nucleic acid comprises a sequence with at least 70% identity to Strand Ref.: 23 or 26.~~

~~178. The RNA targeting molecule of claim 133, or any other prior claim, wherein the double-stranded RNA duplex comprises:~~

~~(a) an RNA strand comprising a sequence according to Strand Ref.: 24 or 27; and~~

~~(b) an RNA strand comprising a sequence according to Strand Ref.: 25 or 28;~~

~~and wherein, the at least one single-stranded guide nucleic acid comprises a sequence according to Strand Ref.: 23 or 26.~~

~~179. The RNA targeting molecule of any one of claims 133-176, wherein the double-stranded RNA duplex comprises:~~

~~(a) an RNA strand comprising a sequence with at least 70% identity to Strand Ref.: 353 or 355; and~~

~~(b) an RNA strand comprising a sequence with at least 70% identity to Strand Ref.: 815 or 818.~~

~~180. The RNA targeting molecule of any one of claims 133-176, wherein the double-stranded RNA duplex comprises:~~

~~(a) an RNA strand comprising a sequence according to Strand Ref.: 353 or 355; and~~

~~(b) an RNA strand comprising a sequence according to Strand Ref.: 815 or 818.~~

~~181. The RNA targeting molecule of any one of claims 133-176, wherein the double-stranded RNA duplex comprises:~~

~~(a) an RNA strand comprising a sequence with at least 70% identity to Strand Ref.: 641 or 643; and~~

~~(b) an RNA strand comprising a sequence with at least 70% identity to Strand Ref.: 841 or 869.~~

~~182. The RNA targeting molecule of any one of claims 133-176, wherein the double-stranded RNA duplex comprises:~~

~~(a) an RNA strand comprising a sequence according to Strand Ref.: 641 or 643; and~~

~~(b) an RNA strand comprising a sequence according to Strand Ref.: 841 or 869.~~

~~183. The RNA targeting molecule of claim 133, or any other prior claim, comprising two or more double-stranded RNA duplexes.~~

~~184. The RNA targeting molecule of claim 133, or any other prior claims, comprising two or more single-stranded guide nucleic acids.~~

~~185. The RNA targeting molecule of claim 133, or any other prior claim, comprising 2-10 double-stranded RNA duplexes.~~

~~186. The RNA targeting molecule of claim 133, or any other prior claims, comprising 2-10 single-stranded guide nucleic acids.~~

~~187. The RNA targeting molecule of claim 133, or any other prior claim, comprising 2-5 double-stranded RNA duplexes.~~

~~188. The RNA targeting molecule of claim 133, or any other prior claims, comprising 2-5 single-stranded guide nucleic acids.~~

~~189. The RNA targeting molecule of any one of claims 133-188, wherein one strand of the double-stranded RNA duplex is not covalently connected to the other strand of the RNA duplex.~~

~~190. The RNA targeting molecule of any one of claims 133-189, wherein the double-stranded RNA duplex does not comprise a hairpin connecting one strand of the RNA duplex to the other strand of the RNA duplex.~~

~~191. The RNA targeting molecule of any one of claims 133-190, wherein the double-stranded RNA duplex comprises two RNA strands having an equal number of nucleotides.~~

~~192. The RNA targeting molecule of any one of claims 133-191, wherein the double-stranded RNA duplex comprises two RNA strands having a different number of nucleotides.~~

~~193. The RNA targeting molecule of any one of claims 133-192, wherein the linker does not comprise a nucleotide or nucleoside.~~

~~194. The RNA targeting molecule of any one of claims 133-193, wherein the linker is a non-nucleic acid linker.~~

~~195. An RNA targeting molecule comprising:~~

~~(a) a first double-stranded RNA duplex comprising two RNA strands;~~

~~(b) a second double-stranded RNA duplex comprising two RNA strands;~~

~~(b) a single-stranded guide nucleic acid; and~~

~~(c) a linker;~~

~~wherein the first double-stranded RNA duplex is connected to the second double-stranded RNA duplex via the linker.~~

~~196. An RNA targeting molecule comprising:~~

~~(a) a double-stranded RNA duplex comprising two RNA strands;~~

~~(b) a first single-stranded guide nucleic acid;~~

~~(c) a second single-stranded guide nucleic acid; and~~

~~(c) a linker;~~

~~wherein the first single-stranded guide nucleic acid is connected to the second single-stranded guide nucleic acid via the linker.~~

~~197. The RNA targeting molecule of claim 133, or any other prior claim, wherein the double-stranded RNA duplex comprises at least one mismatch.~~

~~198. The RNA targeting molecule of claim 133, or any other prior claim, wherein the single-stranded guide nucleic acid comprises at least two mismatches relative to a target sequence.~~