CLAIMS

1. An oligonucleotide for target-editing, or a pharmaceutically acceptable salt thereof, comprising:

a first oligonucleotide identifying a target RNA; and

a second oligonucleotide linked to the 5'-side of the first oligonucleotide, wherein the first oligonucleotide consists of

a target-corresponding nucleotide residue corresponding to an adenosine residue in the target RNA,

an oligonucleotide of 10 to 24 residues, linked to the 3'-side of the target-corresponding nucleotide residue and having a base sequence complementary to the target RNA, and

an oligonucleotide of 3 to 6 residues, linked to the 5'-side of the target-corresponding nucleotide residue and having a base sequence complementary to the target RNA,

the second oligonucleotide has no nucleotide residue corresponding to a nucleotide residue of the target RNA or has a nucleotide residue which does not form a complementary pair with a nucleotide residue of the target RNA, at the 3'-end thereof,

a number of residues in the second oligonucleotide is 2 to 10, and at least the nucleotide residues other than at the 3'-end form a double-stranded structure complementary to the target RNA,

a counter region consisting of the target-corresponding nucleotide residue and each one residue at the 3'-side and the 5'-side thereof is contained,

the nucleotide residue linked to the 3'-side of the target-corresponding nucleotide residue is a 2'-deoxynucleotide residue,

the third nucleotide residue counted in the 3'-direction from the target-corresponding nucleotide in the oligonucleotide linked to the 3'-side of the target-corresponding nucleotide residue is a 2'-deoxy-2'-fluoronucleotide residue, and

the oligonucleotide, or a pharmaceutically acceptable salt thereof induces site-specific editing for the target RNA.

2. The oligonucleotide for target-editing, or a pharmaceutically acceptable salt thereof, according to claim 1, wherein the number of residues in the second oligonucleotide is 4 to 8.

3. The oligonucleotide for target-editing, or a pharmaceutically acceptable salt thereof, according to claim 1 or 2, wherein the 3'-end of the second oligonucleotide has no nucleotide residue corresponding to a nucleotide residue of the target RNA.

4. The oligonucleotide for target-editing, or a pharmaceutically acceptable salt thereof, according to any one of claims 1 to 3, wherein the site-specific editing is due to an enzyme reaction by adenosine deaminase 1.

5. The oligonucleotide for target-editing, or a pharmaceutically acceptable salt thereof, according to any one of claims 1 to 4, comprising a linking portion containing an alkyleneoxy unit between the first oligonucleotide and the second oligonucleotide.

6. The oligonucleotide for target-editing, or a pharmaceutically acceptable salt thereof, according to any one of claims 1 to 5, wherein the first oligonucleotide contains a phosphorothioate bond.

7. The oligonucleotide for target-editing, or a pharmaceutically acceptable salt thereof, according to any one of claims 1 to 6, wherein the first oligonucleotide contains at least one modified nucleotide residue selected from the group consisting of a 2'-O-alkyl ribonucleotide residue, a 2'-deoxy-2'-fluoro ribonucleotide residue, a bridged nucleotide residue, and a 2'-deoxyribonucleotide.

8. The oligonucleotide for target-editing, or a pharmaceutically acceptable salt thereof, according to any one of claims 1 to 7, wherein the counter region contains a phosphorothioate bond.

9. The oligonucleotide for target-editing, or a pharmaceutically acceptable salt thereof, according to any one of claims 1 to 8, wherein the target-corresponding nucleotide residue contains a phosphorothioate bond.

10. The oligonucleotide for target-editing, or a pharmaceutically acceptable salt thereof, according to any one of claims 1 to 9, wherein the nucleotide residue linked to the 5'-side of the target-corresponding nucleotide residue is a 2'-O-alkyl ribonucleotide residue or a deoxynucleotide residue.

11. The oligonucleotide for target-editing, or a pharmaceutically acceptable salt thereof, according to any one of claims 1 to 10, wherein the second oligonucleotide contains at least one modified nucleotide residue selected from the group consisting of a 2'-O-alkyl ribonucleotide residue, a 2'-deoxy-2'-fluoro ribonucleotide residue, and a bridged nucleotide residue.

12. The oligonucleotide for target-editing, or a pharmaceutically acceptable salt thereof, according to any one of claims 1 to 11, wherein the oligonucleotide linked to the 3'-side of the target-corresponding nucleotide residue has a base sequence in which a 2'-deoxy-2'-fluoronucleotide residue and a 2'-O-alkyl ribonucleotide residue are alternately linked.

13. The oligonucleotide for target-editing, or a pharmaceutically acceptable salt thereof, according to any one of claims 1 to 12, wherein the oligonucleotide linked to the 3'-side of the target-corresponding nucleotide residue has a base sequence in which a bridged nucleotide residue and a 2'-O-alkyl ribonucleotide residue are alternately linked.

14. The oligonucleotide for target-editing, or a pharmaceutically acceptable salt thereof, according to any one of claims 1 to 13, wherein the oligonucleotide linked to the 3'-side of the target-corresponding nucleotide residue has a base sequence in which a 2'-deoxy-2'-fluoronucleotide residue and a bridged nucleotide residue are alternately linked.

15. The oligonucleotide for target-editing, or a pharmaceutically acceptable salt thereof, according to any one of claims 1 to 14, wherein an oligonucleotide linked to the 5'-side of the target-corresponding nucleotide residue in the first oligonucleotide has a base sequence in which a 2'-O-alkyl ribonucleotide residue is linked.

16. The oligonucleotide for target-editing, or a pharmaceutically acceptable salt thereof, according to any one of claims 1 to 15, wherein an oligonucleotide linked to the 5'-side of the target-corresponding nucleotide residue in the first oligonucleotide has a base sequence in which a 2'-O-alkyl ribonucleotide residue and a bridged nucleotide residue are alternately linked.

17. The oligonucleotide for target-editing, or a pharmaceutically acceptable salt thereof, according to any one of claims 1 to 16, wherein an oligonucleotide linked to the 5'-side of the target-corresponding nucleotide residue in the first oligonucleotide has a base sequence in which a 2'-O-alkyl ribonucleotide residue and a 2'-deoxy-2'-fluoronucleotide residue are alternately linked.

18. The oligonucleotide for target-editing, or a pharmaceutically acceptable salt thereof, according to any one of claims 1 to 17, wherein the second oligonucleotide has a base sequence in which a 2'-O-alkyl ribonucleotide residue is linked.

19. The oligonucleotide for target-editing, or a pharmaceutically acceptable salt thereof, according to any one of claims 1 to 18, wherein the second oligonucleotide has a base sequence in which a 2'-O-alkyl ribonucleotide residue and a bridged nucleotide residue are alternately linked.

20. The oligonucleotide for target-editing, or a pharmaceutically acceptable salt thereof, according to any one of claims 1 to 19, wherein the second oligonucleotide has a base sequence in which a 2'-O-alkyl ribonucleotide residue and a 2'-deoxy-2'-fluoronucleotide residue are alternately linked.

21. The oligonucleotide for target-editing, or a pharmaceutically acceptable salt thereof, according to any one of claims 1 to 20, wherein

a cytidine residue is linked to the 5'-side of the adenosine residue to be edited in the target RNA, and

the nucleotide residue linked to the 3'-side of the target-corresponding nucleotide residue in the first oligonucleotide is a 2'-deoxyinosine residue.

22. The oligonucleotide for target-editing, or a pharmaceutically acceptable salt thereof, according to any one of claims 1 to 20, wherein

a uridine residue is linked to the 5'-side of the adenosine residue to be edited in the target RNA, and

the nucleotide residue linked to the 3'-side of the target-corresponding nucleotide residue in the first oligonucleotide is a 2'-deoxyadenosine residue.

23. The oligonucleotide for target-editing, or a pharmaceutically acceptable salt thereof, according to any one of claims 1 to 20, wherein

an adenosine residue is linked to the 5'-side of the adenosine residue to be edited in the target RNA, and

the nucleotide residue linked to the 3'-side of the target-corresponding nucleotide residue in the first oligonucleotide is a thymidine residue or a 2'-deoxyuridine residue.

24. The oligonucleotide for target-editing, or a pharmaceutically acceptable salt thereof, according to any one of claims 1 to 20, wherein

a guanosine residue is linked to the 5'-side of the adenosine residue to be edited in the target RNA, and

the nucleotide residue linked to the 3'-side of the target-corresponding nucleotide residue in the first oligonucleotide is a 2'-deoxyinosine residue.

25. The oligonucleotide for target-editing, or a pharmaceutically acceptable salt thereof, according to any one of claims 1 to 24, wherein the target-corresponding

nucleotide residue is an *N*-alkylpyrimidine nucleotide residue or a 2'-deoxycytidine residue.

26. The oligonucleotide for target-editing, or a pharmaceutically acceptable salt thereof, according to any one of claims 1 to 25, wherein the first oligonucleotide and the second oligonucleotide are each formed by linking nucleotide residues by a phosphorothioate bond.

27. The oligonucleotide for target-editing, or a pharmaceutically acceptable salt thereof, according to any one of claims 1 to 26, wherein the first oligonucleotide contains a bridged nucleotide residue in the tenth or subsequent nucleotide residues counted in the 3'-direction from the target-corresponding nucleotide.

28. The oligonucleotide for target-editing, or a pharmaceutically acceptable salt thereof, according to claim 27, wherein an oligonucleotide composed of the tenth or subsequent nucleotide residues counted in the 3'-direction from the target-corresponding nucleotide in the first oligonucleotide has a base sequence in which a 2'-O-alkyl ribonucleotide residue and a bridged nucleotide residue are alternately linked.

29. The oligonucleotide for target-editing, or a pharmaceutically acceptable salt thereof, according to any one of claims 1 to 28, wherein the second oligonucleotide contains a bridged nucleotide residue in the second or subsequent nucleotide residues counted in the 5'-direction from the nucleotide residue at the 3'-end thereof.

30. The oligonucleotide for target-editing, or a pharmaceutically acceptable salt thereof, according to claim 29, wherein an oligonucleotide composed of the second or

subsequent nucleotide residues counted in the 5'-direction from the nucleotide residue at the 3'-end of the second oligonucleotide has a base sequence in which a 2'-O-alkyl ribonucleotide residue and a bridged nucleotide residue are alternately linked.

31. The oligonucleotide for target-editing, or a pharmaceutically acceptable salt thereof, according to any one of claims 1 to 30, represented by any of the following formulae:

U(M)^T(L)^G(M)^A(L)^U(M)^G(F)^A(F)^C(M)^C(M)^c^i^G(M)^U(F)^G(M)^G(F)^C(M)^A(F)^U(M)^C(F)^A(M)^G(L)^U(M)^T(L)^G(M) (AD1_ASS1.39)

A(M)^A(L)^G(M)^A(L)^A(M)^A(F)^U(F)^U(M)^C(M)^c^a^A(M)^C(F)^A(M)^A(F)^A(M)^U(F)^A(M)^C(F)^C(M)^A(L)^C(M)^C(L)^U(M) (AD1_PANK2.39)

A(M)^T(L)^G(M)^T(L)^C(M)^C(F)^A(F)^G(M)^U(M)^c^i^G(M)^A(F)^A(M)^U(F)^A(M)^U(F)^A(M)^A(F)^U(M)^T(L)^A(M)^C(L)^U(M) (AD1_NPHS2.39)

G(M)^C(L)^A(M)^T(L)^C(M)^C(F)^U(F)^G(M)^C(M)^c^i^C(M)^A(F)^U(M)^A(F)^A(M)^A(F)^G(M)^G(F)^C(M)^A(L)^C(M)^C(L)^C(M) (AD1_GRIA2.39)

U(M)^G(L)^A(M)^U(L)^G(F)^A(F)^C(M)^C(M)^c^i^G(M)^U(F)^G(M)^G(F)^C(M)^A(F)^U(M)^C(F)^A(L)^G(M)^U(L)^U(M) (AD1_ASS1.52)

G(M)^C(E)^A(M)^T(E)^C(M)^C(F)^U(F)^G(M)^C(M)^c^i^C(M)^A(F)^U(M)^A(F)^A(M)^A(F)^G(M)^G(F)^C(M)^A(E)^C(M)^C(E)^C(M) (AD1_GRIA2.39e)

U(M)^T(E)^G(M)^A(E)^U(M)^G(F)^A(F)^C(M)^C(M)^c^i^G(M)^U(F)^G(M)^G(F)^C(M)^A(F)^U(M)^C(F)^A(M)^G(E)^U(M)^T(E)^G(M) (AD1_ASS1.39e)

A(M)^A(E)^G(M)^A(E)^A(M)^A(F)^U(F)^U(M)^C(M)^c^a^A(M)^C(F)^A(M)^A(F)^A(M)^U(F)^A(M)^C(F)^C(M)^A(E)^C(M)^C(E)^U(M) (AD1_PANK2.39e)

A(M)^T(E)^G(M)^T(E)^C(M)^C(F)^A(F)^G(M)^U(M)^c^i^G(M)^A(F)^A(M)^U(F)^A(M)^U(F)^A(M)^A(F)^U(M)^T(E)^A(M)^C(E)^U(M) (AD1_NPHS2.39e)

C(M)^A(E)^U(M)^C(E)^C(F)^U(F)^G(M)^C(M)^c^i^C(M)^A(F)^U(M)^A(F)^A(M)^A(F)^G(M)^G(F)^C(E)^A(M)^C(E)^C(M)) (AD1_GRIA2.52e)

U(M)^G(E)^A(M)^T(E)^G(F)^A(F)^C(M)^C(M)^c^i^G(M)^U(F)^G(M)^G(F)^C(M)^A(F)^U(M)^C(F)^A(E)^G(M)^T(E)^U(M) (AD1_ASS1.52e)

A(M)^G(E)^A(M)^A(E)^A(F)^U(F)^U(M)^C(M)^c^a^A(M)^C(F)^A(M)^A(F)^A(M)^U(F)^A(M)^C(F)^C(E)^A(M)^C(E)^C(M) (AD1_PANK2.52e)

U(M)^G(E)^U(M)^C(E)^C(F)^A(F)^G(M)^U(M)^c^i^G(M)^A(F)^A(M)^U(F)^A(M)^U(F)^A(M)^A(F)^T(E)^U(M)^A(E)^C(M) (AD1_NPHS2.52e)

G(M)^T(L)^C(M)^C(L)^C(M)^U(F)^U(F)^C(M)^U(M)^c^i^U(M)^C(F)^G(M)^A(F)^U(M)^G(F)^G(M)^U(F)^C(M)^A(L)^G(M)^C(L)^A(M) (AD1_A1AT.39)

wherein a capital letter denotes a ribonucleotide residue, a small letter represents a 2'-deoxyribonucleotide residue, N(M) represents a 2'-O-methyl- ribonucleotide residue, N(F) represents a 2'-fluoro-2'-deoxyribonucleotide residue, N(L) represents a 2'-O,4'-C-methylenated ribonucleotide residue, N(E) represents a 2'-O,4'-C-ethylenated ribonucleotide residue, and "^" represents that nucleoside units are linked by -P(=S)(OH)-.

32. The oligonucleotide for target-editing, or a pharmaceutically acceptable salt thereof, according to any one of claims 1 to 31, wherein a delivery molecule containing GalNAc, cholesterol, and a fatty acid is bound via a linker or a phosphodiester bond (including a phosphorothioate bond) at the 5'-end or the 3'-end of the oligonucleotide and the pharmaceutically acceptable salt thereof.

33. A hereditary disease therapeutic agent comprising the oligonucleotide, or a pharmaceutically acceptable salt thereof, according to any one of claims 1 to 32, for use in the treatment of a disease associated with the target RNA.

34. A pharmaceutical composition comprising the oligonucleotide, or a pharmaceutically acceptable salt thereof, according to any one of claims 1 to 32, as an active component, for use in the therapy of a disease associated with the target RNA.

35. A~~The~~ pharmaceutical composition comprising the oligonucleotide, or a pharmaceutically acceptable salt thereof, according to any one of claims 1 to 32~~34~~, for use in the prevention or therapy of a hereditary disease.

36. The pharmaceutical composition for use according to claim 35, wherein the hereditary disease is a disease curable by conversion of an adenosine residue into an inosine residue in the target RNA.

37. The pharmaceutical composition for use according to claim 35, wherein the hereditary disease is a hereditary disease caused by mutation of a guanosine residue to an adenosine residue in a gene.

38. Use of the oligonucleotide, or a pharmaceutically acceptable salt thereof, according to any one of claims 1 to 32, in~~for~~ production of a medicine for prevention or therapy of a disease associated with the target RNA.

39. The oligonucleotide, or a pharmaceutically acceptable salt thereof, according to any one of claims 1 to 32, for use in the prevention or therapy of a disease associated with the target RNA.

40. Use of~~A method comprising administering~~ a pharmacologically effective amount of the oligonucleotide, or a pharmaceutically acceptable salt thereof, according to any one

of claims 1 to 32, in the manufacture of a medicament~~to a warm-blooded animal,~~ to prevent or cure a disease associated with the target RNA, wherein the medicament is to be administered to a warm-blooded animal.

41. The ~~method~~ use according to claim 40, wherein the disease is a hereditary disease.

42. The ~~method~~ use according to claim 41, wherein the hereditary disease is a disease curable by conversion of an adenosine residue into an inosine residue in the target RNA.

43. The ~~method~~ use according to claim 41, wherein the hereditary disease is a hereditary disease caused by mutation of a guanosine residue to an adenosine residue in a gene.

44. The pharmaceutical composition for use according to any one of claims 34 to 37, wherein the disease comprises at least one selected from the group consisting of type I citrullinemia, hemophilia (thrombosis), ALS, pantothenic acid-related neurodegenerative disease, homocystinuria, focal segmental glomerulosclerosis, α1 anti-trypsin deficiency, phenyl ketonuria, pachydermoperiostosis, Alexander disease, primary hyperoxaluria, Gilbert syndrome, retinitis pigmentosa, distal myopathy, and hemochromatosis.

45. The use of the oligonucleotide, or a pharmaceutically acceptable salt thereof, according to claim 38, wherein the disease comprises at least one selected from the group consisting of type I citrullinemia, hemophilia (thrombosis), ALS, pantothenic acid-related neurodegenerative disease, homocystinuria, focal segmental glomerulosclerosis, α1 anti-trypsin deficiency, phenyl ketonuria, pachydermoperiostosis, Alexander disease, primary

hyperoxaluria, Gilbert syndrome, retinitis pigmentosa, distal myopathy, and hemochromatosis.

46. The oligonucleotide, or a pharmaceutically acceptable salt thereof, for use according to claim 39, wherein the disease comprises at least one selected from the group consisting of type I citrullinemia, hemophilia (thrombosis), ALS, pantothenic acid-related neurodegenerative disease, homocystinuria, focal segmental glomerulosclerosis, α1 anti-trypsin deficiency, phenyl ketonuria, pachydermoperiostosis, Alexander disease, primary hyperoxaluria, Gilbert syndrome, retinitis pigmentosa, distal myopathy, and hemochromatosis.

47. The ~~method~~ use according to any one of claims 40 to 43, wherein the disease comprises at least one selected from the group consisting of type I citrullinemia, hemophilia (thrombosis), ALS, pantothenic acid-related neurodegenerative disease, homocystinuria, focal segmental glomerulosclerosis, α1 anti-trypsin deficiency, phenyl ketonuria, pachydermoperiostosis, Alexander disease, primary hyperoxaluria, Gilbert syndrome, retinitis pigmentosa, distal myopathy, and hemochromatosis.