CLAIMS

1. A method for targeted editing of a target RNA in a cell based on the LEAPER technology in vitro or ex vivo, wherein the target RNA comprises a transcript sequence of an α-L-iduronidase (IDUA) gene containing a guanosine (G) to adenosine (A) mutation site (target adenosine), and the method comprises:

introducing into the cell an arRNA or a construct comprising the arRNA coding sequence, wherein the arRNA comprises a complementary RNA sequence that hybridizes to the target RNA, and wherein the arRNA is capable of recruiting an adenosine deaminase acting on RNA (ADAR) by hybridization to the target RNA so as to deaminate the target adenosine in the target RNA, particularly, wherein the nucleotide (targeting nucleotide) in the arRNA opposite to the target adenosine is a cytidine (C), an adenosine (A) or a uridine (U).

~~2. The method according to claim 1, wherein the nucleotide (targeting nucleotide) in the arRNA opposite to the target adenosine is a cytidine (C), an adenosine (A) or a uridine (U).~~

~~3~~2. The method according to claim 1 ~~or 2~~, wherein the target adenosine forms a target triplet together with its 5' most adjacent nucleotide and 3' most adjacent nucleotide, and the target triplet is 5'-UAG-3', particularly, wherein the 5' most adjacent nucleotide of the targeting nucleotide is a cytidine (C), a guanosine (G) or a uridine (U).

~~4. The method according to any one of claims 1-3, wherein the 5' most adjacent nucleotide of the targeting nucleotide is a cytidine (C), a guanosine (G) or a uridine (U).~~

~~5~~3. The method according to any one of claims 1-~~4~~2, wherein the 3' most adjacent nucleotide of the targeting nucleotide is an adenosine (A), particularly, wherein the targeting nucleotide forms a targeting triplet together with its 5' most adjacent nucleotide and 3' most adjacent nucleotide, and the targeting triplet is 5'-CCA-3'.

~~6. The method according to any one of claims 1-5, wherein the targeting nucleotide forms a~~

~~targeting triplet together with its 5' most adjacent nucleotide and 3' most adjacent nucleotide, and the targeting triplet is 5'-CCA-3'.~~

~~7~~4. The method according to any one of claims 1-~~6~~3, wherein the length of the arRNA is any integer number of nt selected from 61nt to 121nt.

~~8~~5. The method according to any one of claims 1-~~7~~4, wherein the distance from the targeting nucleotide of the arRNA to the 3' end of the arRNA is less than the distance from the targeting nucleotide to the 5' end of the arRNA, particularly, wherein the distance from the targeting nucleotide of the arRNA to the 3' end of the arRNA is any integer number of nt selected from 9nt to 60nt, or, wherein the distance from the targeting nucleotide of the arRNA to the 5' end of the arRNA is any integer number of nt selected from 25nt to 60nt.

~~9. The method according to any one of claims 1-8, wherein the distance from the targeting nucleotide of the arRNA to the 3' end of the arRNA is any integer number of nt selected from 9nt to 60nt.~~

~~10. The method according to any one of claims 1-9, wherein the distance from the targeting nucleotide of the arRNA to the 5' end of the arRNA is any integer number of nt selected from 25nt to 60nt.~~

~~11~~6. The method according to any one of claims 1-~~10~~5, wherein the arRNA is an arRNA having a length characteristic selected from the group consisting of:

55nt-c-35nt, 55nt-c-25nt, 55nt-c-24nt, 55nt-c-21nt, 55nt-c-20nt, 55nt-c-19nt, 55nt-c-18nt, 55nt-c-17nt, 55nt-c-16nt, 55nt-c-15nt, 55nt-c-14nt, 55nt-c-13nt, 55nt-c-12nt, 55nt-c-11nt, 55nt-c-10nt, 55nt-c-9nt, 50nt-c-20nt, 50nt-c-15nt, and 45nt-c-20nt;

wherein cytidine is the targeting nucleotide in the arRNA opposite to the target adenosine, and the orientation of the arRNA is 5' to 3'.

~~12. The method according to any one of claims 1-11, wherein the arRNA is an arRNA having a~~

~~length charactorastic selected from the group consisting of: 55nt-c-20nt, 55nt-c-15nt, and 55nt-c-14nt.~~

~~13~~7. The method according to any one of claims 1-12, wherein the arRNA comprises one or more chemical modifications,

particularly, the chemical modification is one or more selected from the group consisting of:

2'-O-methylation modification, phosphorothioation modification in internucleotide linkage, deoxyribonucleotide substitution modification, LNA modification, and 2'-O-(2-methoxyethyl) modification,

more particularly,

the chemical modification is one or more selected from the group consisting of:

1) 2'-O-methylation modifications in the first 2, 3, 4 or 5 nucleotides;

2) 2'-O-methylation modifications in the last 2, 3, 4, or 5 nucleotides;

3) 2'-O-methylation modifications in all the cytidines except that in the targeting triplet;

4) 2'-O-(2-methoxyethyl) modifications in the first 2, 3 or 4 nucleotides;

5) 2'-O-(2-methoxyethyl) modifications in the last 2, 3 or 4 nucleotides;

6) deoxyribonucleotide substitution modifications of the first 2, 3 or 4 nucleotides;

7) deoxyribonucleotide substitution modifications of the last 2, 3 or 4 nucleotides;

8) phosphorothioation modifications in the first 1, 2, 3, 4 or 5 internucleotide linkages;

9) phosphorothioation modifications in the last 1, 2, 3, 4 or 5 internucleotide linkages;

10) phosphorothioation modifications in all internucleotide linkages except that one or more of the 5' or 3' most adjacent internucleotide linkages of each of the nucleotides in the targeting triplet are not modified by phosphorothioation; and

(11) phosphorothioation modifications in internucleotide linkages at an interval of 1, 2, 3, or 4 nucleotides except that one or more of the 5' or 3' most adjacent internucleotide linkages of each of the nucleotides in the targeting triplet are not modified by phosphorothioation.~~.~~

~~14. The method according to claim 13, wherein the chemical modification is one or more selected from the group consisting of:~~

~~2'-O-methylation modification, phosphorothioation modification in internucleotide linkage, deoxyribonucleotide substitution modification, LNA modification, and 2'-O-(2-methoxyethyl)~~

~~modification.~~

~~15. The method according to claim 13 or 14, wherein the chemical modification is one or more selected from the group consisting of:~~

~~1) 2'-O-methylation modifications in the first 2, 3, 4 or 5 nucleotides;~~

~~2) 2'-O-methylation modifications in the last 2, 3, 4, or 5 nucleotides;~~

~~3) 2'-O-methylation modifications in all the cytidines except that in the targeting triplet;~~

~~4) 2'-O-(2-methoxyethyl) modifications in the first 2, 3 or 4 nucleotides;~~

~~5) 2'-O-(2-methoxyethyl) modifications in the last 2, 3 or 4 nucleotides;~~

~~6) deoxyribonucleotide substitution modifications of the first 2, 3 or 4 nucleotides;~~

~~7) deoxyribonucleotide substitution modifications of the last 2, 3 or 4 nucleotides;~~

~~8) phosphorothioation modifications in the first 1, 2, 3, 4 or 5 internucleotide linkages;~~

~~9) phosphorothioation modifications in the last 1, 2, 3, 4 or 5 internucleotide linkages;~~

~~10) phosphorothioation modifications in all internucleotide linkages except that one or more of the 5' or 3' most adjacent internucleotide linkages of each of the nucleotides in the targeting triplet are not modified by phosphorothioation; and~~

~~(11) phosphorothioation modifications in internucleotide linkages at an interval of 1, 2, 3, or 4 nucleotides except that one or more of the 5' or 3' most adjacent internucleotide linkages of each of the nucleotides in the targeting triplet are not modified by phosphorothioation.~~

~~16~~8. The method according to ~~any one of~~ claim~~s 13-15~~ 7, wherein the arRNA comprises any chemical modification selected from the group consisting of:

CM0: the first 3 and the last 3 nucleotides in the arRNA sequence are respectively modified by 2'-O-methylation, and the first 3 and the last 3 internucleotide linkages in the arRNA sequence are respectively modified by phosphorothioation;

CM1: the first 3 and the last 3 nucleotides in the arRNA sequence are respectively modified by 2'-O-methylation, the first 3 and the last 3 internucleotide linkages in the arRNA sequence are respectively modified by phosphorothioation, and all the uridines of the sequence are modified by 2'-O-methylation;

CM2: the first 3 and the last 3 nucleotides in the arRNA sequence are respectively modified by

2'-O-methylation, and the first 3 and last 3 internucleotide linkages in the arRNA sequence are respectively modified by phosphorothioation; and the 3' most adjacent nucleotide of the targeting nucleotide is modified by 2'-O-methylation;

CM3: the first 3 and the last 3 nucleotides in the arRNA sequence are respectively modified by 2'-O-methylation, and the first 3 and the last 3 internucleotide linkages in the arRNA sequence are respectively modified by phosphorothioation; and the 5' most adjacent nucleotide of the targeting nucleotide is modified by 2'-O-methylation;

CM4: the first 3 and the last 3 nucleotides in the arRNA sequence are respectively modified by 2'-O-methylation, and the first 3 and the last 3 internucleotide linkages in the arRNA sequence are respectively modified by phosphorothioation; and the 3' most adjacent internucleotide linkage of each of the three bases in the targeting triplet is respectively modified by phosphorothioation;

CM6: the first 5 and the last 5 nucleotides in the arRNA sequence are respectively modified by 2'-O-methylation, and the first 5 and the last 5 internucleotide linkages in the arRNA sequence are respectively modified by phosphorothioation;

CM148: the first 4 and the last 4 nucleotides in the arRNA sequence are respectively modified by 2'-O-(2-methoxyethyl), the first 3 and the last 4 internucleotide linkages in the arRNA sequence are respectively modified by phosphorothioation, and all the uridines of the sequence are modified by 2'-O-Me;

CM149: the first 3 and the last 3 nucleotides in the arRNA sequence are respectively modified by 2'-O-(2-methoxyethyl), the first 2 and the last 3 internucleotide linkages in the arRNA sequence are respectively modified by phosphorothioation, and all the uridines of the sequence are modified by 2'-O-Me;

CM150: the first 2 and the last 2 nucleotides in the arRNA sequence are respectively modified by 2'-O-(2-methoxyethyl), the first 1 and the last 2 internucleotide linkages in the arRNA sequence are respectively modified by phosphorothioation, and all the uridines of the sequence are modified by 2'-O-Me;

CM151: the first 4 and the last 4 nucleotides in the arRNA sequence are respectively modified by LNA, the first 3 and the last 4 internucleotide linkages in the arRNA sequence are respectively modified by phosphorothioation, and all the uridines of the sequence are modified by 2'-O-Me;

CM152: the first 3 and the last 3 nucleotides in the arRNA sequence are respectively modified by

LNA, the first 2 and the last 3 internucleotide linkages in the arRNA sequence are respectively modified by phosphorothioation, and all the uridines of the sequence are modified by 2'-O-Me;

CM153: the first 2 and the last 2 nucleotides in the arRNA sequence are respectively modified by LNA, the first 2 and the last 3 internucleotide linkages in the arRNA sequence are respectively modified by phosphorothioation, and all the uridines of the sequence are modified by 2'-O-Me;

CM94: the first 3 and the last 3 nucleotides in the arRNA sequence, all the uridines and all the cytidines except that in the targeting triplet in the arRNA sequence are modified by 2'-O-methylation; the first 4 and the last 3 internucleotide linkages in the arRNA sequence are all modified by phosphorothioation; and from the 4th internucleotide linkage from the 5' end to the 3rd internucleotide linkage from the 3' end, every other internucleotide linkage is modified by phosphorothioation, except that the 5' most adjacent internucleotide linkage of each nucleotide in the targeting triple is not modified by phosphorothioation;

CM119: the first 3 and the last 3 nucleotides in the arRNA sequence, all the uridines and all the cytidines in the arRNA sequence except that in the targeting triplet are modified by 2'-O-methylation; the first 4 and the last 3 internucleotide linkages in the arRNA sequence are all modified by phosphorothioation; from the 4th internucleotide linkage from the 5' end to the 3' most adjacent internucleotide linkage of the targeting nucleotide, and from the 3rd internucleotide linkage from the 3' end to the 3’ most adjacent nucleotide of the targeting nucleotide, every other internucleotide linkage is modified by phosphorothioation; and the targeting nucleotide is substituted by a deoxyribonucleotide;

CM120: the first 3 and the last 3 nucleotides in the arRNA sequence, all the uridines and all the cytidines in the arRNA sequence except that in the targeting triplet are modified by 2'-O-methylation; the first 4 and the last 3 internucleotide linkages in the arRNA sequence are modified by phosphorothioation; from the 4th internucleotide linkage from the 5' end to the 5' most adjacent internucleotide linkage of the targeting nucleotide, and from the 3rd internucleotide linkage from the 3' end to the 3’ most adjacent internucleotide linkage of the targeting nucleotide, every other internucleotide linkage is modified by phosphorothioation; and the targeting nucleotide is substituted by a deoxyribonucleotide;

CM123: the first 3 and the last 3 nucleotides in the arRNA sequence, all the uridines and all the cytidines in the arRNA sequence except that in the targeting triplet are modified by 2'-O-methylation;

the first 4 and the last 3 internucleotide linkages are modified by phosphorothioation; from the 4th internucleotide linkage from the 5' end to the 3' most adjacent internucleotide linkage of the targeting nucleotide, and from the 3rd internucleotide linkage from the 3' end to the 3' most adjacent nucleotide of the targeting nucleotide, every other internucleotide linkage is modified by phosphorothioation; and each nucleotide in the targeting triplet is substituted by a deoxyribonucleotide;

CM125: the first 3 and the last 3 nucleotides in the arRNA sequence, all the uridines and all the cytidines in the arRNA sequence except that in the targeting triplet are modified by 2'-O-methylation; the first 4 and the last 3 internucleotide linkages and the 3' most adjacent nucleotide linkages of the target nucleotide are modified by phosphorothioation; from the 4th internucleotide linkage from the 5' end to the 5' most adjacent nucleotide of the targeting nucleotide's 5' most adjacent nucleotide, and from the 3rd internucleotide linkage from the 3' end to the 3' most adjacent nucleotide of the targeting nucleotide, every other internucleotide linkage is modified by phosphorothioation; and each nucleotide in the targeting triplet is substituted by a deoxyribonucleotide.

~~179~~. The method according to any one of claims 1-~~168~~, wherein the guanosine (G) to adenosine (A) mutation site targeted by the arRNA is a mutation site in NM_000203.4(IDUA)-c.1205G>A (p.Trp402Ter), or a corresponding mutation site thereof, in the genome of a patient with Hurler syndrome, particularly, wherein the arRNA comprises any sequence selected from the group consisting of:

1)Gm*Am*Cm-G*Cm-Cm*Cm-A*Cm-Cm*G-Um*G-Um*G-G*Um-Um*G-Cm*Um-G*Um-Cm*Cm-A*G-G*A-Cm*G-G*Um-Cm*Cm-Cm*G-G*Cm-Cm*Um-G*Cm-G*A-Cm*A-Cm*Um-Um*Cm-G*G-Cm-C-C-A*G-A*G-Cm*Um-G*Cm-Um*Cm-Cm*Um*Cm*Am (SEQ ID NO: 31);

2)Gm*Am*Cm-G*Cm-Cm*Cm-A*-Cm-Cm*G-Um*G-Um*G-G*Um-Um*G-Cm*Um-G*Um-Cm*Cm-A*G-G*A-Cm*G-G*Um-Cm*Cm-Cm*G-G*Cm-Cm*Um-G*Cm-G*-A-Cm*A-Cm*Um-Um*Cm-G*G-Cm*Cd-Cd*Ad*-G-A*G-Cm*Um-G*Cm-Um*Cm-Cm*Um*Cm*Am (SEQ ID NO: 31);

3)Gm*Am*Cm-G*Cm-Cm*Cm-A*Cm-Cm*G-Um*G-Um*G-G*Um-Um*G-Cm*Um-G*Um-Cm*Cm-A*G-G*A-Cm*-G-G*Um-Cm*Cm-Cm*G-G*Cm-Cm*Um-G*-Cm-G*A-Cm*A-Cm*Um-Um*Cm-G*G-Cm-Cd-Cd*Ad*G-A*G-Cm*Um-G*Cm-Um*Cm-Cm*Um*Cm*Am (SEQ ID NO: 31);

4)Gmoe*Amoe*Cmoe*Gmoe-C-C-C-A-C-C-G-Um-G-Um-G-G-Um-Um-G-C-Um-G-Um-C-C-A-G-G-A-C-G-G-Um-C-C-C-G-G-C-C-Um-GC-G-A-C-A-C-Um-Um-C-G-G-C-C-C-A-G-A-G-C-Um-G-C-Um-C*Cmoe*Umoe*Cmoe*Amoe (SEQ ID NO: 31); or

5)G+*A+*C+*G+C-C-C-A-C-C-G-Um-G-Um-G-G-Um-Um-G-C-Um-G-Um-C-C-A-G-G-A-C-G-G-Um-C-C-C-G-G-C-C-Um-GC-G-A-C-A-C-Um-Um-C-G-G-C-C-C-A-G-A-G-C-Um-G-C-Um-C*C+*U+*C+*A+ (SEQ ID NO: 31);

wherein * indicates a phosphorothioation modification, m indicates a 2'-O-methylation modification, moe indicates a 2'-O-(2-methoxyethyl) modification, + indicates an LNA modification, and d indicates a deoxyribonucleotide substitution modification.

~~18. The method according to any one of claims 1-17, wherein the arRNA comprises any sequence selected from the group consisting of:~~

~~1)Gm*Am*Cm-G*Cm-Cm*Cm-A*Cm-Cm*G-Um*G-Um*G-G*Um-Um*G-Cm*Um-G*Um-Cm*Cm-A*G-G*A-Cm*G-G*Um-Cm*Cm-Cm*G-G*Cm-Cm*Um-G*Cm-G*A-Cm*A-Cm*Um-Um*Cm-G*G-Cm-C-C-A*G-A*G-Cm*Um-G*Cm-Um*Cm-Cm*Um*Cm*Am (SEQ ID NO: 31);~~

~~2)Gm*Am*Cm-G*Cm-Cm*Cm-A*-Cm-Cm*G-Um*G-Um*G-G*Um-Um*G-Cm*Um-G*Um-Cm*Cm-A*G-G*A-Cm*G-G*Um-Cm*Cm-Cm*G-G*Cm-Cm*Um-G*Cm-G*-A-Cm*A-Cm*Um-Um*Cm-G*G-Cm*Cd-Cd*Ad*-G-A*G-Cm*Um-G*Cm-Um*Cm-Cm*Um*Cm*Am (SEQ ID NO: 31);~~

~~3)Gm*Am*Cm-G*Cm-Cm*Cm-A*Cm-Cm*G-Um*G-Um*G-G*Um-Um*G-Cm*Um-G*Um-Cm*Cm-A*G-G*A-Cm*-G-G*Um-Cm*Cm-Cm*G-G*Cm-Cm*Um-G*-Cm-G*A-Cm*A-Cm*Um-Um*Cm-G*G-Cm-Cd-Cd*Ad*G-A*G-Cm*Um-G*Cm-Um*Cm-Cm*Um*Cm*Am (SEQ ID NO: 31);~~

~~4)Gmoe*Amoe*Cmoe*Gmoe-C-C-C-A-C-C-G-Um-G-Um-G-G-Um-Um-G-C-Um-G-Um-C-C-A-G-G-A-C-G-G-Um-C-C-C-G-G-C-C-Um-GC-G-A-C-A-C-Um-Um-C-G-G-C-C-C-A-G-A-G-C-Um-G-C-Um-C*Cmoe*Umoe*Cmoe*Amoe (SEQ ID NO: 31); or~~

~~5)G+*A+*C+*G+C-C-C-A-C-C-G-Um-G-Um-G-G-Um-Um-G-C-Um-G-Um-C-C-A-G-G-A-C-G-G-Um-C-C-C-G-G-C-C-Um-GC-G-A-C-A-C-Um-Um-C-G-G-C-C-C-A-G-A-G-C-Um-G-C-Um-C*C+*U+*C+*A+ (SEQ ID NO: 31);~~

~~wherein * indicates a phosphorothioation modification, m indicates a 2'-O-methylation~~

~~modification, moe indicates a 2'-O-(2-methoxyethyl) modification, + indicates an LNA modification, and d indicates a deoxyribonucleotide substitution modification.~~

~~19~~10. The method according to any one of claims 1-~~18~~9, wherein the arRNA is introduced into the cells by any method selected from the group consisting of: electroporation, liposome transfection, exosome delivery, or lipid-nanoparticle delivery (LNP), particularly, wherein the amount of arRNA in a single introduction into the cells is 5 to 160 nM, more particularly, wherein several introductions are taken for introducing the arRNA into the cells, and the interval between the adjacent two introductions is ≤ 21 days.

~~20. The method according to any one of claims 1-19, wherein the amount of arRNA in a single introduction into the cells is 5 to 160 nM.~~

~~21. The method according to any one of claims 1-20, wherein several introductions are taken for introducing the arRNA into the cells, and the interval between the adjacent two introductions is ≤ 21 days.~~

~~22. A method for preventing or treating Hurler syndrome, comprising correcting a pathogenic G>A mutation of Hurler syndrome by using the method according to any one of claims 1-21.~~

~~23~~11. An engineered arRNA ~~which is used for~~for use in targeted editing of a target RNA in a cell based on LEAPER technology, wherein the target RNA comprises a transcript sequence of an α-L-iduronidase (IDUA) gene containing a guanosine (G) to adenosine (A) mutation site (target adenosine), the arRNA comprises a complementary RNA sequence that hybridizes to the target RNA, and the arRNA is capable of recruiting an adenosine deaminase acting on RNA (ADAR) by hybridization to the target RNA so as to deaminate the target adenosine in the target RNA, the guanosine (G) to adenosine (A) mutation site targeted by the arRNA is NM_000203.4(IDUA)-c.1205G>A (p.Trp402Ter) mutation site, or a corresponding mutation site thereof, in the genome of a patient with Hurler syndrome.

~~24~~12. The arRNA according to claim ~~23~~11, wherein the arRNA is an arRNA having a length charactorastic selected from the group consisting of:

55nt-c-35nt, 55nt-c-25nt, 55nt-c-24nt, 55nt-c-21nt, 55nt-c-20nt, 55nt-c-19nt, 55nt-c-18nt, 55nt-c-17nt, 55nt-c-16nt, 55nt-c-15nt, 55nt-c-14nt, 55nt-c-13nt, 55nt-c-12nt, 55nt-c-11nt, 55nt-c-10nt, 55nt-c-9nt, 50nt-c-20nt, 50nt-c-15nt, and 45nt-c-20nt;

wherein cytidine is the targeting nucleotide in the arRNA opposite to the target adenosine, and the orientation of the arRNA is 5' to 3'.

~~25~~13. The arRNA according to claim ~~23~~11 or ~~24~~12, wherein the arRNA comprises one or more chemical modifications, particularly, the chemical modification is one or more selected from the group consisting of:

2'-O-methylation modification, phosphorothioation modification in internucleotide linkage, deoxyribonucleotide substitution modification, LNA modification, and 2'-O-(2-methoxyethyl) modification,

more particularly, the chemical modification is one or more selected from the group consisting of:

1) 2'-O-methylation modifications in the first 2, 3, 4 or 5 nucleotides;

2) 2'-O-methylation modifications in the last 2, 3, 4, or 5 nucleotides;

3) 2'-O-methylation modifications in all the cytidines except that in the targeting triplet;

4) 2'-O-(2-methoxyethyl) modifications in the first 2, 3 or 4 nucleotides;

5) 2'-O-(2-methoxyethyl) modifications in the last 2, 3 or 4 nucleotides;

6) deoxyribonucleotide substitution modifications of the first 2, 3 or 4 nucleotides;

7) deoxyribonucleotide substitution modifications of the last 2, 3 or 4 nucleotides;

8) phosphorothioation modifications in the first 1, 2, 3, 4 or 5 internucleotide linkages;

9) phosphorothioation modifications in the last 1, 2, 3, 4 or 5 internucleotide linkages;

10) phosphorothioation modifications in all internucleotide linkages except that one or more of the 5' or 3' most adjacent internucleotide linkages of each of the nucleotides in the targeting triplet are not modified by phosphorothioation; and

(11) phosphorothioation modifications in internucleotide linkages at an interval of 1, 2, 3, or 4 nucleotides except that one or more of the 5' or 3' most adjacent internucleotide linkages of each of the

nucleotides in the targeting triplet are not modified by phosphorothioation,

even more particularly, the arRNA comprises any chemical modification selected from the group consisting of:

CM0: the first 3 and the last 3 nucleotides in the arRNA sequence are respectively modified by 2'-O-methylation, and the first 3 and the last 3 internucleotide linkages in the arRNA sequence are respectively modified by phosphorothioation;

CM1: the first 3 and the last 3 nucleotides in the arRNA sequence are respectively modified by 2'-O-methylation, the first 3 and the last 3 internucleotide linkages in the arRNA sequence are respectively modified by phosphorothioation, and all the uridines of the sequence are modified by 2'-O-methylation;

CM2: the first 3 and the last 3 nucleotides in the arRNA sequence are respectively modified by 2'-O-methylation, and the first 3 and last 3 internucleotide linkages in the arRNA sequence are respectively modified by phosphorothioation; and the 3' most adjacent nucleotide of the targeting nucleotide is modified by 2'-O-methylation;

CM3: the first 3 and the last 3 nucleotides in the arRNA sequence are respectively modified by 2'-O-methylation, and the first 3 and the last 3 internucleotide linkages in the arRNA sequence are respectively modified by phosphorothioation; and the 5' most adjacent nucleotide of the targeting nucleotide is modified by 2'-O-methylation;

CM4: the first 3 and the last 3 nucleotides in the arRNA sequence are respectively modified by 2'-O-methylation, and the first 3 and the last 3 internucleotide linkages in the arRNA sequence are respectively modified by phosphorothioation; and the 3' most adjacent internucleotide linkage of each of the three bases in the targeting triplet is modified by phosphorothioation;

CM6: the first 5 and the last 5 nucleotides in the arRNA sequence are respectively modified by 2'-O-methylation, and the first 5 and the last 5 internucleotide linkages in the arRNA sequence are respectively modified by phosphorothioation;

CM148: the first 4 and the last 4 nucleotides in the arRNA sequence are respectively modified by 2'-O-(2-methoxyethyl), the first 3 and the last 4 internucleotide linkages in the arRNA sequence are respectively modified by phosphorothioation, and all the uridines of the sequence are modified by 2'-O-Me;

CM149: the first 3 and the last 3 nucleotides in the arRNA sequence are respectively modified by

2'-O-(2-methoxyethyl), the first 2 and the last 3 internucleotide linkages in the arRNA sequence are respectively modified by phosphorothioation, and all the uridines of the sequence are modified by 2'-O-Me;

CM150: the first 2 and the last 2 nucleotides in the arRNA sequence are respectively modified by 2'-O-(2-methoxyethyl), the first 1 and the last 2 internucleotide linkages in the arRNA sequence are respectively modified by phosphorothioation, and all the uridines of the sequence are modified by 2'-O-Me;

CM151: the first 4 and the last 4 nucleotides in the arRNA sequence are respectively modified by LNA, the first 3 and the last 4 internucleotide linkages in the arRNA sequence are respectively modified by phosphorothioation, and all the uridines of the sequence are modified by 2'-O-Me;

CM152: the first 3 and the last 3 nucleotides in the arRNA sequence are respectively modified by LNA, the first 2 and the last 3 internucleotide linkages in the arRNA sequence are respectively modified by phosphorothioation, and all the uridines of the sequence are modified by 2'-O-Me;

CM153: the first 2 and the last 2 nucleotides in the arRNA sequence are respectively modified by LNA, the first 2 and the last 3 internucleotide linkages in the arRNA sequence are respectively modified by phosphorothioation, and all the uridines of the sequence are modified by 2'-O-Me;

CM94: the first 3 and the last 3 nucleotides in the arRNA sequence, all the uridines and all the cytidines except that in the targeting triplet in the arRNA sequence are modified by 2'-O-methylation; the first 4 and the last 3 internucleotide linkages in the arRNA sequence are all modified by phosphorothioation; from the 4th internucleotide linkage from the 5' end to the 3rd internucleotide linkage from the 3' end, every other internucleotide linkage is modified by phosphorothioation, except that the 5' most adjacent internucleotide linkage of each nucleotide in the targeting triple is not modified by phosphorothioation;

CM119: the first 3 and the last 3 nucleotides in the arRNA sequence, all the uridines and all the cytidines in the arRNA sequence except that in the targeting triplet, are modified by 2'-O-methylation; the first 4 and the last 3 internucleotide linkages in the arRNA sequence are all modified by phosphorothioation; from the 4th internucleotide linkage from the 5' end to the 3' most adjacent internucleotide linkage of the targeting nucleotide, and from the 3rd internucleotide linkage from the 3' end to the 3’ most adjacent nucleotide of the targeting nucleotide, every other internucleotide linkage is modified by phosphorothioation; and the targeting nucleotide is substituted by a

deoxyribonucleotide;

CM120: the first 3 and the last 3 nucleotides in the arRNA sequence, all the uridines and all the cytidines in the arRNA sequence except that in the targeting triplet are modified by 2'-O-methylation; the first 4 and the last 3 internucleotide linkages in the arRNA sequence are modified by phosphorothioation; from the 4th internucleotide linkage from the 5' end to the 5' most adjacent internucleotide linkage of the targeting nucleotide, and from the 3rd internucleotide linkage from the 3' end to the 3’ most adjacent internucleotide linkage of the targeting nucleotide, every other internucleotide linkage is modified by phosphorothioation; and the targeting nucleotide is substituted by a deoxyribonucleotide;

CM123: the first 3 and the last 3 nucleotides in the arRNA sequence, all the uridines and all the cytidines in the arRNA sequence except that in the targeting triplet are modified by 2'-O-methylation; the first 4 and the last 3 internucleotide linkages are modified by phosphorothioation; from the 4th internucleotide linkage from the 5' end to the 3' most adjacent internucleotide linkage of the targeting nucleotide, and from the 3rd internucleotide linkage from the 3' end to the 3’ most adjacent nucleotide of the targeting nucleotide, every other internucleotide linkage is modified by phosphorothioation; and each nucleotide in the targeting triplet is substituted by a deoxyribonucleotide;

CM125: the first 3 and the last 3 nucleotides in the arRNA sequence, all the uridines and all the cytidines in the arRNA sequence except that in the targeting triplet are modified by 2'-O-methylation; the first 4 and the last 3 internucleotide linkages and the 3' most adjacent nucleotide linkages of the targeting nucleotide are modified by phosphorothioation; from the 4th internucleotide linkage from the 5' end to the 5' most adjacent nucleotide of the targeting nucleotide’s 5' most adjacent nucleotide, and from the 3rd internucleotide linkage from the 3' end to the 3’ most adjacent nucleotide of the targeting nucleotide, every other internucleotide linkage is modified by phosphorothioation; and each nucleotide in the targeting triplet is substituted by a deoxyribonucleotide,

specifically, the arRNA comprises any sequence selected from the group consisting of:

1)Gm*Am*Cm*G*Cm-Cm*Cm-A*Cm-Cm*G-Um*G-Um*G-G*Um-Um*G-Cm*Um-G*Um-Cm*Cm-A*G-G*A-Cm*G-G*Um-Cm*Cm-Cm*G-G*Cm-Cm*Um-G*Cm-G*A-Cm*A-Cm*Um-Um*Cm-G*G-Cm-C-C-A*G-A*G-Cm*Um-G*Cm-Um*Cm-Cm*Um*Cm*Am (SEQ ID NO: 31);

2)Gm*Am*Cm*G*Cm-Cm*Cm-A*-Cm-Cm*G-Um*G-Um*G-G*Um-Um*G-Cm*Um-G*Um-Cm*Cm-A*G-G*A-Cm*G-G*Um-Cm*Cm-Cm*G-G*Cm-Cm*Um-G*Cm-G*-A-Cm*A-Cm*Um-

Um*Cm-G*G-Cm*Cd-Cd*Ad*-G-A*G-Cm*Um-G*Cm-Um*Cm-Cm*Um*Cm*Am (SEQ ID NO: 31);

3)Gm*Am*Cm*G*Cm-Cm*Cm-A*Cm-Cm*G-Um*G-Um*G-G*Um-Um*G-Cm*Um-G*Um-Cm*Cm-A*G-G*A-Cm*-G-G*Um-Cm*Cm-Cm*G-G*Cm-Cm*Um-G*-Cm-G*A-Cm*A-Cm*Um-Um*Cm-G*G-Cm-Cd-Cd*Ad*G-A*G-Cm*Um-G*Cm-Um*Cm-Cm*Um*Cm*Am (SEQ ID NO: 31);

4)Gmoe*Amoe*Cmoe*Gmoe-C-C-C-A-C-C-G-Um-G-Um-G-G-Um-Um-G-C-Um-G-Um-C-C-A-G-G-A-C-G-G-Um-C-C-C-G-G-C-C-Um-GC-G-A-C-A-C-Um-Um-C-G-G-C-C-C-A-G-A-G-C-Um-G-C-Um-C*Cmoe*Umoe*Cmoe*Amoe (SEQ ID NO: 31); or

5)G+*A+*C+*G+C-C-C-A-C-C-G-Um-G-Um-G-G-Um-Um-G-C-Um-G-Um-C-C-A-G-G-A-C-G-G-Um-C-C-C-G-G-C-C-Um-GC-G-A-C-A-C-Um-Um-C-G-G-C-C-C-A-G-A-G-C-Um-G-C-Um-C*C+*U+*C+*A+ (SEQ ID NO: 31);

wherein * indicates a phosphorothioation modification, m indicates a 2'-O-methylation modification, moe indicates a 2'-O-(2-methoxyethyl) modification, + indicates an LNA modification, and d indicates a deoxyribonucleotide substitution modification.

~~26. The arRNA according to any one of claims 23-25, wherein the chemical modification is one or more selected from the group consisting of:~~

~~2'-O-methylation modification, phosphorothioation modification in internucleotide linkage, deoxyribonucleotide substitution modification, LNA modification, and 2'-O-(2-methoxyethyl) modification.~~

~~27. The arRNA according to any one of claims 23-26, wherein the chemical modification is one or more selected from the group consisting of:~~

~~1) 2'-O-methylation modifications in the first 2, 3, 4 or 5 nucleotides;~~

~~2) 2'-O-methylation modifications in the last 2, 3, 4, or 5 nucleotides;~~

~~3) 2'-O-methylation modifications in all the cytidines except that in the targeting triplet;~~

~~4) 2'-O-(2-methoxyethyl) modifications in the first 2, 3 or 4 nucleotides;~~

~~5) 2'-O-(2-methoxyethyl) modifications in the last 2, 3 or 4 nucleotides;~~

~~6) deoxyribonucleotide substitution modifications of the first 2, 3 or 4 nucleotides;~~

7) deoxyribonucleotide substitution modifications of the last 2, 3 or 4 nucleotides;

8) phosphorothioation modifications in the first 1, 2, 3, 4 or 5 internucleotide linkages;

9) phosphorothioation modifications in the last 1, 2, 3, 4 or 5 internucleotide linkages;

10) phosphorothioation modifications in all internucleotide linkages except that one or more of the 5' or 3' most adjacent internucleotide linkages of each of the nucleotides in the targeting triplet are not modified by phosphorothioation; and

(11) phosphorothioation modifications in internucleotide linkages at an interval of 1, 2, 3, or 4 nucleotides except that one or more of the 5' or 3' most adjacent internucleotide linkages of each of the nucleotides in the targeting triplet are not modified by phosphorothioation.

28. The arRNA according to any one of claims 23-27, wherein the arRNA comprises any chemical modification selected from the group consisting of:

CM0: the first 3 and the last 3 nucleotides in the arRNA sequence are respectively modified by 2'-O-methylation, and the first 3 and the last 3 internucleotide linkages in the arRNA sequence are respectively modified by phosphorothioation;

CM1: the first 3 and the last 3 nucleotides in the arRNA sequence are respectively modified by 2'-O-methylation, the first 3 and the last 3 internucleotide linkages in the arRNA sequence are respectively modified by phosphorothioation, and all the uridines of the sequence are modified by 2'-O-methylation;

CM2: the first 3 and the last 3 nucleotides in the arRNA sequence are respectively modified by 2'-O-methylation, and the first 3 and last 3 internucleotide linkages in the arRNA sequence are respectively modified by phosphorothioation; and the 3' most adjacent nucleotide of the targeting nucleotide is modified by 2'-O-methylation;

CM3: the first 3 and the last 3 nucleotides in the arRNA sequence are respectively modified by 2'-O-methylation, and the first 3 and the last 3 internucleotide linkages in the arRNA sequence are respectively modified by phosphorothioation; and the 5' most adjacent nucleotide of the targeting nucleotide is modified by 2'-O-methylation;

CM4: the first 3 and the last 3 nucleotides in the arRNA sequence are respectively modified by 2'-O-methylation, and the first 3 and the last 3 internucleotide linkages in the arRNA sequence are respectively modified by phosphorothioation; and the 3' most adjacent internucleotide linkage of each

~~of the three bases in the targeting triplet is modified by phosphorothioation;~~

~~CM6: the first 5 and the last 5 nucleotides in the arRNA sequence are respectively modified by 2'-O-methylation, and the first 5 and the last 5 internucleotide linkages in the arRNA sequence are respectively modified by phosphorothioation;~~

~~CM148: the first 4 and the last 4 nucleotides in the arRNA sequence are respectively modified by 2'-O-(2-methoxyethyl), the first 3 and the last 4 internucleotide linkages in the arRNA sequence are respectively modified by phosphorothioation, and all the uridines of the sequence are modified by 2'-O-Me;~~

~~CM149: the first 3 and the last 3 nucleotides in the arRNA sequence are respectively modified by 2'-O-(2-methoxyethyl), the first 2 and the last 3 internucleotide linkages in the arRNA sequence are respectively modified by phosphorothioation, and all the uridines of the sequence are modified by 2'-O-Me;~~

~~CM150: the first 2 and the last 2 nucleotides in the arRNA sequence are respectively modified by 2'-O-(2-methoxyethyl), the first 1 and the last 2 internucleotide linkages in the arRNA sequence are respectively modified by phosphorothioation, and all the uridines of the sequence are modified by 2'-O-Me;~~

~~CM151: the first 4 and the last 4 nucleotides in the arRNA sequence are respectively modified by LNA, the first 3 and the last 4 internucleotide linkages in the arRNA sequence are respectively modified by phosphorothioation, and all the uridines of the sequence are modified by 2'-O-Me;~~

~~CM152: the first 3 and the last 3 nucleotides in the arRNA sequence are respectively modified by LNA, the first 2 and the last 3 internucleotide linkages in the arRNA sequence are respectively modified by phosphorothioation, and all the uridines of the sequence are modified by 2'-O-Me;~~

~~CM153: the first 2 and the last 2 nucleotides in the arRNA sequence are respectively modified by LNA, the first 2 and the last 3 internucleotide linkages in the arRNA sequence are respectively modified by phosphorothioation, and all the uridines of the sequence are modified by 2'-O-Me;~~

~~CM94: the first 3 and the last 3 nucleotides in the arRNA sequence, all the uridines and all the cytidines except that in the targeting triplet in the arRNA sequence are modified by 2'-O-methylation; the first 4 and the last 3 internucleotide linkages in the arRNA sequence are all modified by phosphorothioation; from the 4th internucleotide linkage from the 5' end to the 3rd internucleotide linkage from the 3' end, every other internucleotide linkage is modified by phosphorothioation,~~

except that the 5' most adjacent internucleotide linkage of each nucleotide in the targeting triple is not modified by phosphorothioation;

CM119: the first 3 and the last 3 nucleotides in the arRNA sequence, all the uridines and all the cytidines in the arRNA sequence except that in the targeting triplet, are modified by 2'-O-methylation; the first 4 and the last 3 internucleotide linkages in the arRNA sequence are all modified by phosphorothioation; from the 4th internucleotide linkage from the 5' end to the 3' most adjacent internucleotide linkage of the targeting nucleotide, and from the 3rd internucleotide linkage from the 3' end to the 3’ most adjacent nucleotide of the targeting nucleotide, every other internucleotide linkage is modified by phosphorothioation; and the targeting nucleotide is substituted by a deoxyribonucleotide;

CM120: the first 3 and the last 3 nucleotides in the arRNA sequence, all the uridines and all the cytidines in the arRNA sequence except that in the targeting triplet are modified by 2'-O-methylation; the first 4 and the last 3 internucleotide linkages in the arRNA sequence are modified by phosphorothioation; from the 4th internucleotide linkage from the 5' end to the 5' most adjacent internucleotide linkage of the targeting nucleotide, and from the 3rd internucleotide linkage from the 3' end to the 3’ most adjacent internucleotide linkage of the targeting nucleotide, every other internucleotide linkage is modified by phosphorothioation; and the targeting nucleotide is substituted by a deoxyribonucleotide;

CM123: the first 3 and the last 3 nucleotides in the arRNA sequence, all the uridines and all the cytidines in the arRNA sequence except that in the targeting triplet are modified by 2'-O-methylation; the first 4 and the last 3 internucleotide linkages are modified by phosphorothioation; from the 4th internucleotide linkage from the 5' end to the 3' most adjacent internucleotide linkage of the targeting nucleotide, and from the 3rd internucleotide linkage from the 3' end to the 3’ most adjacent nucleotide of the targeting nucleotide, every other internucleotide linkage is modified by phosphorothioation; and each nucleotide in the targeting triplet is substituted by a deoxyribonucleotide;

CM125: the first 3 and the last 3 nucleotides in the arRNA sequence, all the uridines and all the cytidines in the arRNA sequence except that in the targeting triplet are modified by 2'-O-methylation; the first 4 and the last 3 internucleotide linkages and the 3' most adjacent nucleotide linkages of the targeting nucleotide are modified by phosphorothioation; from the 4th internucleotide linkage from the 5' end to the 5' most adjacent nucleotide of the targeting nucleotide’s 5' most adjacent nucleotide,

and from the 3rd internucleotide linkage from the 3' end to the 3' most adjacent nucleotide of the targeting nucleotide, every other internucleotide linkage is modified by phosphorothioation; and each nucleotide in the targeting triplet is substituted by a deoxyribonucleotide.

29. The arRNA according to any one of claims 23-28, wherein the arRNA comprises any sequence selected from the group consisting of:

1)Gm*Am*Cm*G*Cm-Cm*Cm-A*Cm-Cm*G-Um*G-Um*G-G*Um-Um*G-Cm*Um-G*Um-Cm*Cm-A*G-G*A-Cm*G-G*Um-Cm*Cm-Cm*G-G*Cm-Cm*Um-G*Cm-G*A-Cm*A-Cm*Um-Um*Cm-G*G-Cm-C-C-A*G-A*G-Cm*Um-G*Cm-Um*Cm-Cm*Um*Cm*Am (SEQ ID NO: 31);

2)Gm*Am*Cm*G*Cm-Cm*Cm-A*-Cm-Cm*G-Um*G-Um*G-G*Um-Um*G-Cm*Um-G*Um-Cm*Cm-A*G-G*A-Cm*G-G*Um-Cm*Cm-Cm*G-G*Cm-Cm*Um-G*Cm-G*-A-Cm*A-Cm*Um-Um*Cm-G*G-Cm*Cd-Cd*Ad*-G-A*G-Cm*Um-G*Cm-Um*Cm-Cm*Um*Cm*Am (SEQ ID NO: 31);

3)Gm*Am*Cm*G*Cm-Cm*Cm-A*Cm-Cm*G-Um*G-Um*G-G*Um-Um*G-Cm*Um-G*Um-Cm*Cm-A*G-G*A-Cm*-G-G*Um-Cm*Cm-Cm*G-G*Cm-Cm*Um-G*-Cm-G*A-Cm*A-Cm*Um-Um*Cm-G*G-Cm-Cd-Cd*Ad*G-A*G-Cm*Um-G*Cm-Um*Cm-Cm*Um*Cm*Am (SEQ ID NO: 31);

4)Gmoe*Amoe*Cmoe*Gmoe-C-C-C-A-C-C-G-Um-G-Um-G-G-Um-Um-G-C-Um-G-Um-C-C-A-G-G-A-C-G-G-Um-C-C-C-G-G-C-C-Um-GC-G-A-C-A-C-Um-Um-C-G-G-C-C-C-A-G-A-G-C-Um-G-C-Um-C*Cmoe*Umoe*Cmoe*Amoe (SEQ ID NO: 31); or

5)G+*A+*C+*G+C-C-C-A-C-C-G-Um-G-Um-G-G-Um-Um-G-C-Um-G-Um-C-C-A-G-G-A-C-G-G-Um-C-C-C-G-G-C-C-Um-GC-G-A-C-A-C-Um-Um-C-G-G-C-C-C-A-G-A-G-C-Um-G-C-Um-C*C+*U+*C+*A+ (SEQ ID NO: 31);

wherein * indicates a phosphorothioation modification, m indicates a 2'-O-methylation modification, moe indicates a 2'-O-(2-methoxyethyl) modification, + indicates an LNA modification, and d indicates a deoxyribonucleotide substitution modification.

30. A construct comprising the coding sequence of the arRNA according to claim 23 or 24.

14. 31. A parmaceutical composition, liposome, exosome, lipid nanoparticle, cell, library, or kit

comprising the arRNA according to any one of claims 11-13~~23-29 or the construct according to claim 30~~.

~~14.~~15. The arRNA according to any one of claims 11-13 for use in preventing or treating Hurler syndrome, comprising correcting a pathogenic G>A mutation of Hurler syndrome.