CLAIMS:

1. A replication-defective adeno-associated virus (AAV) comprising:
    a) an AAV capsid comprising an AAV Clade F capsid protein; and
    b) a correction genome comprising from 5' to 3':
        (i) a 5' AAV ITR nucleotide sequence;
        (ii) a 5' homology arm nucleotide sequence of up to 2000 nucleotides in length, comprising a nucleotide sequence that is at least 95% identical to nucleotides 1 to 800 of SEQ ID NO: 31;
        (iii) an editing element for editing a target locus in an HBB gene, comprising a nucleotide sequence that encodes the amino acid sequence set forth in SEQ ID NO: 48;
        (iv) a 3' homology arm nucleotide sequence of up to 2000 nucleotides in length, comprising a nucleotide sequence that is at least 95% identical to nucleotides 133 to 232 of SEQ ID NO: 102; and
        (v) a 3' AAV ITR nucleotide sequence.

2. The AAV of claim 1, wherein:

each of the 5' and 3' homology arm nucleotide sequences independently has a length of about 100 to about 2000 nucleotides;

the 5' homology arm nucleotide sequence comprises a nucleotide sequence that is at least 99% identical to nucleotides 1 to 800 of SEQ ID NO: 31, or comprises nucleotides 1 to 800 of SEQ ID NO: 31; and/or

the 3' homology arm nucleotide sequence comprises a nucleotide sequence that is at least 99% identical to nucleotides 133 to 232 of SEQ ID NO: 102, or comprises nucleotides 133 to 232 of SEQ ID NO: 102.

3. The AAV of claim 1 or 2, wherein the editing element comprises a nucleotide sequence that is at least 90% identical to nucleotides 801 to 2356 of SEQ ID NO: 32, optionally wherein:

the editing element comprises nucleotides 801 to 2356 of SEQ ID NO: 32, optionally wherein the correction genome comprises the nucleotide sequence set forth in any one of SEQ ID NOs: 30, 32, 36; or

the editing element comprises nucleotides 801 to 2356 of SEQ ID NO: 34, optionally wherein the correction genome comprises the nucleotide sequence set forth in SEQ ID NO: 34 or 38.

4. The AAV of any one of the preceding claims, wherein:

the 5' AAV ITR nucleotide sequence has at least 95% sequence identity to SEQ ID NO: 18, and the 3' AAV ITR nucleotide sequence has at least 95% sequence identity to SEQ ID NO: 19; or

the 5' AAV ITR nucleotide sequence has at least 95% sequence identity to SEQ ID NO: 20, and the 3' AAV ITR nucleotide sequence has at least 95% sequence identity to SEQ ID NO: 21.

5. The AAV of any one of the preceding claims, wherein the AAV Clade F capsid protein comprises an AAV capsid protein comprising:

an amino acid sequence having at least 90% sequence identity with the amino acid sequence of amino acids 203-736 of SEQ ID NO: 2, 3, 4, 6, 7, 10, 11, 12, 13, 15, 16, or 17, optionally wherein:

(i) the amino acid in the capsid protein corresponding to amino acid 206 of SEQ ID NO: 2 is C; the amino acid in the capsid protein corresponding to amino acid 296 of SEQ ID NO: 2 is H; the amino acid in the capsid protein corresponding to amino acid 312 of SEQ ID NO: 2 is Q; the amino acid in the capsid protein corresponding to amino acid 346 of SEQ ID NO: 2 is A; the amino acid in the capsid protein corresponding to amino acid 464 of SEQ ID NO: 2 is N; the amino acid in the capsid protein corresponding to amino acid 468 of SEQ ID NO: 2 is S; the amino acid in the capsid protein corresponding to amino acid 501 of SEQ ID NO: 2 is I; the amino acid in the capsid protein corresponding to amino acid 505 of SEQ ID NO: 2 is R; the amino acid in the capsid protein corresponding to amino acid 590 of SEQ ID NO: 2 is R; the amino acid in the capsid protein corresponding to amino acid 626 of SEQ ID NO: 2 is G or Y; the amino acid in the capsid protein corresponding to amino acid 681 of SEQ ID NO: 2 is M; the amino acid in the capsid protein corresponding to amino acid 687 of SEQ ID NO: 2 is R; the amino acid in the capsid protein corresponding to amino acid 690 of SEQ ID NO: 2 is K; the amino acid in the capsid protein corresponding to amino acid 706 of SEQ ID

NO: 2 is C; or, the amino acid in the capsid protein corresponding to amino acid 718 of SEQ ID NO: 2 is G;

(ii) (a) the amino acid in the capsid protein corresponding to amino acid 626 of SEQ ID NO: 2 is G, and the amino acid in the capsid protein corresponding to amino acid 718 of SEQ ID NO: 2 is G; (b) the amino acid in the capsid protein corresponding to amino acid 296 of SEQ ID NO: 2 is H, the amino acid in the capsid protein corresponding to amino acid 464 of SEQ ID NO: 2 is N, the amino acid in the capsid protein corresponding to amino acid 505 of SEQ ID NO: 2 is R, and the amino acid in the capsid protein corresponding to amino acid 681 of SEQ ID NO: 2 is M; (c) the amino acid in the capsid protein corresponding to amino acid 505 of SEQ ID NO: 2 is R, and the amino acid in the capsid protein corresponding to amino acid 687 of SEQ ID NO: 2 is R; (d) the amino acid in the capsid protein corresponding to amino acid 346 of SEQ ID NO: 2 is A, and the amino acid in the capsid protein corresponding to amino acid 505 of SEQ ID NO: 2 is R; or (e) the amino acid in the capsid protein corresponding to amino acid 501 of SEQ ID NO: 2 is I, the amino acid in the capsid protein corresponding to amino acid 505 of SEQ ID NO: 2 is R, and the amino acid in the capsid protein corresponding to amino acid 706 of SEQ ID NO: 2 is C; and/or

(iii) the capsid protein comprises the amino acid sequence of amino acids 203-736 of SEQ ID NO: 2, 3, 4, 6, 7, 10, 11, 12, 13, 15, 16, or 17;

an amino acid sequence having at least 90% sequence identity with the amino acid sequence of amino acids 138-736 of SEQ ID NO: 2, 3, 4, 5, 6, 7, 9, 10, 11, 12, 13, 15, 16, or 17, optionally wherein:

(i) the amino acid in the capsid protein corresponding to amino acid 151 of SEQ ID NO: 2 is R; the amino acid in the capsid protein corresponding to amino acid 160 of SEQ ID NO: 2 is D; the amino acid in the capsid protein corresponding to amino acid 206 of SEQ ID NO: 2 is C; the amino acid in the capsid protein corresponding to amino acid 296 of SEQ ID NO: 2 is H; the amino acid in the capsid protein corresponding to amino acid 312 of SEQ ID NO: 2 is Q; the amino acid in the capsid protein corresponding to amino acid 346 of SEQ ID NO: 2 is A; the amino acid in the capsid protein corresponding to amino acid 464 of SEQ ID NO: 2 is N; the amino acid in the capsid protein corresponding to amino acid 468 of SEQ ID NO: 2 is S; the amino acid in the capsid protein corresponding to amino acid 501 of SEQ ID NO: 2 is I; the amino acid in the capsid protein corresponding to amino

acid 505 of SEQ ID NO: 2 is R; the amino acid in the capsid protein corresponding to amino acid 590 of SEQ ID NO: 2 is R; the amino acid in the capsid protein corresponding to amino acid 626 of SEQ ID NO: 2 is G or Y; the amino acid in the capsid protein corresponding to amino acid 681 of SEQ ID NO: 2 is M; the amino acid in the capsid protein corresponding to amino acid 687 of SEQ ID NO: 2 is R; the amino acid in the capsid protein corresponding to amino acid 690 of SEQ ID NO: 2 is K; the amino acid in the capsid protein corresponding to amino acid 706 of SEQ ID NO: 2 is C; or, the amino acid in the capsid protein corresponding to amino acid 718 of SEQ ID NO: 2 is G;

(ii) (a) the amino acid in the capsid protein corresponding to amino acid 626 of SEQ ID NO: 2 is G, and the amino acid in the capsid protein corresponding to amino acid 718 of SEQ ID NO: 2 is G; (b) the amino acid in the capsid protein corresponding to amino acid 296 of SEQ ID NO: 2 is H, the amino acid in the capsid protein corresponding to amino acid 464 of SEQ ID NO: 2 is N, the amino acid in the capsid protein corresponding to amino acid 505 of SEQ ID NO: 2 is R, and the amino acid in the capsid protein corresponding to amino acid 681 of SEQ ID NO: 2 is M; (c) the amino acid in the capsid protein corresponding to amino acid 505 of SEQ ID NO: 2 is R, and the amino acid in the capsid protein corresponding to amino acid 687 of SEQ ID NO: 2 is R; (d) the amino acid in the capsid protein corresponding to amino acid 346 of SEQ ID NO: 2 is A, and the amino acid in the capsid protein corresponding to amino acid 505 of SEQ ID NO: 2 is R; or (e) the amino acid in the capsid protein corresponding to amino acid 501 of SEQ ID NO: 2 is I, the amino acid in the capsid protein corresponding to amino acid 505 of SEQ ID NO: 2 is R, and the amino acid in the capsid protein corresponding to amino acid 706 of SEQ ID NO: 2 is C; and/or

(iii) the capsid protein comprises the amino acid sequence of amino acids 138-736 of SEQ ID NO: 2, 3, 4, 5, 6, 7, 9, 10, 11, 12, 13, 15, 16, or 17; and/or

an amino acid sequence having at least 90% sequence identity with the amino acid sequence of amino acids 1-736 of SEQ ID NO: 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 15, 16, or 17, optionally wherein:

(i) the amino acid in the capsid protein corresponding to amino acid 2 of SEQ ID NO: 2 is T; the amino acid in the capsid protein corresponding to amino acid 65 of SEQ ID NO: 2 is I; the amino acid in the capsid protein corresponding to amino acid 68 of SEQ ID NO: 2 is V; the amino acid in the capsid protein corresponding to

amino acid 77 of SEQ ID NO: 2 is R; the amino acid in the capsid protein corresponding to amino acid 119 of SEQ ID NO: 2 is L; the amino acid in the capsid protein corresponding to amino acid 151 of SEQ ID NO: 2 is R; the amino acid in the capsid protein corresponding to amino acid 160 of SEQ ID NO: 2 is D; the amino acid in the capsid protein corresponding to amino acid 206 of SEQ ID NO: 2 is C; the amino acid in the capsid protein corresponding to amino acid 296 of SEQ ID NO: 2 is H; the amino acid in the capsid protein corresponding to amino acid 312 of SEQ ID NO: 2 is Q; the amino acid in the capsid protein corresponding to amino acid 346 of SEQ ID NO: 2 is A; the amino acid in the capsid protein corresponding to amino acid 464 of SEQ ID NO: 2 is N; the amino acid in the capsid protein corresponding to amino acid 468 of SEQ ID NO: 2 is S; the amino acid in the capsid protein corresponding to amino acid 501 of SEQ ID NO: 2 is I; the amino acid in the capsid protein corresponding to amino acid 505 of SEQ ID NO: 2 is R; the amino acid in the capsid protein corresponding to amino acid 590 of SEQ ID NO: 2 is R; the amino acid in the capsid protein corresponding to amino acid 626 of SEQ ID NO: 2 is G or Y; the amino acid in the capsid protein corresponding to amino acid 681 of SEQ ID NO: 2 is M; the amino acid in the capsid protein corresponding to amino acid 687 of SEQ ID NO: 2 is R; the amino acid in the capsid protein corresponding to amino acid 690 of SEQ ID NO: 2 is K; the amino acid in the capsid protein corresponding to amino acid 706 of SEQ ID NO: 2 is C; or, the amino acid in the capsid protein corresponding to amino acid 718 of SEQ ID NO: 2 is G;

(ii) (a) the amino acid in the capsid protein corresponding to amino acid 2 of SEQ ID NO: 2 is T, and the amino acid in the capsid protein corresponding to amino acid 312 of SEQ ID NO: 2 is Q; (b) the amino acid in the capsid protein corresponding to amino acid 65 of SEQ ID NO: 2 is I, and the amino acid in the capsid protein corresponding to amino acid 626 of SEQ ID NO: 2 is Y; (c) the amino acid in the capsid protein corresponding to amino acid 77 of SEQ ID NO: 2 is R, and the amino acid in the capsid protein corresponding to amino acid 690 of SEQ ID NO: 2 is K; (d) the amino acid in the capsid protein corresponding to amino acid 119 of SEQ ID NO: 2 is L, and the amino acid in the capsid protein corresponding to amino acid 468 of SEQ ID NO: 2 is S; (e) the amino acid in the capsid protein corresponding to amino acid 626 of SEQ ID NO: 2 is G, and the amino acid in the capsid protein corresponding to amino acid 718 of SEQ ID NO: 2 is G; (f) the

amino acid in the capsid protein corresponding to amino acid 296 of SEQ ID NO: 2 is H, the amino acid in the capsid protein corresponding to amino acid 464 of SEQ ID NO: 2 is N, the amino acid in the capsid protein corresponding to amino acid 505 of SEQ ID NO: 2 is R, and the amino acid in the capsid protein corresponding to amino acid 681 of SEQ ID NO: 2 is M; (g) the amino acid in the capsid protein corresponding to amino acid 505 of SEQ ID NO: 2 is R, and the amino acid in the capsid protein corresponding to amino acid 687 of SEQ ID NO: 2 is R; (h) the amino acid in the capsid protein corresponding to amino acid 346 of SEQ ID NO: 2 is A, and the amino acid in the capsid protein corresponding to amino acid 505 of SEQ ID NO: 2 is R; or (i) the amino acid in the capsid protein corresponding to amino acid 501 of SEQ ID NO: 2 is I, the amino acid in the capsid protein corresponding to amino acid 505 of SEQ ID NO: 2 is R, and the amino acid in the capsid protein corresponding to amino acid 706 of SEQ ID NO: 2 is C; and/or

(iii) the capsid protein comprises the amino acid sequence of amino acids 1-736 of SEQ ID NO: 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 15, 16, or 17.

6. The AAV of any one of the preceding claims, wherein the integration efficiency of the editing element into the target locus is at least 0.5% or at least 1% when the AAV is contacted *in vitro* in the absence of an exogenous nuclease with a population of $CD34^+$ human stem cells under standard AAV transduction conditions.

7. A pharmaceutical composition comprising an AAV of any one of the preceding claims.

8. A packaging system for recombinant preparation of an AAV, wherein the packaging system comprises:

a) a Rep nucleotide sequence encoding one or more AAV Rep proteins;

b) a Cap nucleotide sequence encoding one or more AAV Clade F capsid proteins as set forth in any one of claims 1-5; and

c) a correction genome as set forth in any one of claims 1-5,

wherein the packaging system is operative in a cell for enclosing the correction genome in the capsid to form the AAV.

9. The packaging system of claim 8, wherein:

a) the packaging system comprises a first vector comprising the Rep nucleotide sequence and the Cap nucleotide sequence, and a second vector comprising the correction genome; and/or

b) the Rep nucleotide sequence encodes an AAV2 Rep protein, wherein the AAV2 Rep protein is 78/68 or Rep 68/52; and/or the AAV2 Rep protein comprises an amino acid sequence having a minimum percent sequence identity to the AAV2 Rep amino acid sequence of SEQ ID NO:22, wherein the minimum percent sequence identity is at least 70% across the length of the amino acid sequence encoding the AAV2 Rep protein.

10. The packaging system of claim 8 or 9, further comprising a third vector, wherein the third vector is a helper virus vector, wherein:

a) the helper virus vector is an independent third vector;

b) the helper virus vector is integral with the first vector;

c) the helper virus vector is integral with the second vector;

d) the third vector comprises genes encoding helper virus proteins; and/or

e) the helper virus is selected from the group consisting of adenovirus, herpes virus, vaccinia virus, and cytomegalovirus (CMV), optionally wherein the helper virus is adenovirus and wherein the adenovirus genome comprises one or more adenovirus RNA genes selected from the group consisting of E1, E2, E4 and VA; or

f) the helper virus is herpes simplex virus (HSV), optionally wherein the HSV genome comprises one or more of HSV genes selected from the group consisting of UL5/8/52, ICPO, ICP4, ICP22 and UL30/UL42.

11. The packaging system of any one of claims 8-10, wherein:

a) the first vector and the third vector are contained within a first transfecting plasmid;

b) the nucleotides of the second vector and the third vector are contained within a second transfecting plasmid;

c) the nucleotides of the first vector and the third vector are cloned into a recombinant helper virus; or

d) the nucleotides of the second vector and the third vector are cloned into a recombinant helper virus.

12. A method for recombinant preparation of an AAV, the method comprising introducing the packaging system of any one of claims 8-11 into a cell under conditions operative for enclosing the correction genome in the capsid to form the AAV.

13. A method for correcting a mutation in a beta globin (HBB) gene in a cell, the method comprising transducing the cell with a replication-defective adeno-associated virus (AAV) of any one of claims 1-6, wherein the cell is transduced without co-transducing or co-administering an exogenous nuclease or a nucleotide sequence that encodes an exogenous nuclease.

14. The method of claim 13, wherein the cell is selected from the group consisting of a pluripotent stem cell, a hematopoietic stem cell, and a $CD34^+$ hematopoietic stem cell, and/or the cell is in a mammalian subject and the AAV is to be administered to the subject in an amount effective to transduce the cell in the subject.

15. Use of a replication-defective AAV in the manufacture of a medicament for treating a subject having a disease or disorder associated with an HBB gene mutation, wherein treating the subject comprises:

a) transducing an erythrocyte progenitor cell from the subject *ex vivo* with a replication-defective AAV of any one of claims 1-6; and

b) the transduced cell is to be administered to the subject,

wherein the cell is transduced without co-transducing an exogenous nuclease or a nucleotide sequence that encodes an exogenous nuclease.

16. The use of claim 15, wherein the erythrocyte progenitor cell is selected from the group consisting of a pluripotent stem cell, a hematopoietic stem cell, and a $CD34^+$ hematopoietic stem cell.

17. Use of a replication-defective AAV in the manufacture of a medicament for treating a disease or disorder in a subject, wherein the replication-defective AAV of any one of claims 1-6 is to be administered to the subject, without co-administering an exogenous nuclease or a nucleotide sequence that encodes an exogenous nuclease.

18. The use of claim 17, wherein the disease or disorder is thalassemia or sickle cell disease, and/or the subject is a human subject.

19. The replication-defective AAV of any one of claims 1-6 for use as a medicament.