CLAIMS

What is claimed is:

1. A zinc finger nuclease (ZFN) comprising first and second ZFNs, the first ZFN comprising the ZFN designated 71557 and the second ZFN comprising the ZFN designated 71728.

2. One or more polynucleotides encoding the first and second ZFNs of claim 1, optionally wherein the one or more polynucleotides are carried on AAV vectors.

3. The one or more polynucleotides of claim 2, wherein a first polynucleotide encoding the first ZFN comprises an AAV vector comprising the sequences as shown in Table 4 and a second polynucleotide encoding the second ZFN comprises an AAV vector comprising the sequences as shown in Table 5.

4. An AAV vector of claim 2 or 3, wherein the AAV vector encoding the first ZFN comprises the sequence shown in SEQ ID NO:43.

5. The AAV vector of claim 2 or 3, wherein the AAV vector encoding the second ZFN comprises the sequence shown in SEQ ID NO:56.

6. A cell comprising one or more ZFNs of claim 1, one or more polynucleotides of any of claims 2 to 3, and/or one or more AAV vectors of claims 4 and 5, optionally a stem cell or precursor cell.

7. A pharmaceutical composition comprising one or more ZFNs of claim 1, one or more polynucleotides of any of claims 2 to 3, one or more AAV vectors of claims 4 and 5 and/or one or more cells of claim 6.

8. Use of one or more ZFNs, one or more polynucleotides, one or more AAV vectors, one or more cells and/or one or more pharmaceutical composition of any of the preceding claims for cleaving an endogenous albumin gene in a subject.

9. The use of claim 8, further comprising administering a donor, optionally carried on an AAV vector, to the subject such that the donor is integrated into the cleaved albumin gene in the subject.

10. A method of cleaving an endogenous albumin gene in a cell of a subject, the method comprising administering one or more ZFNs of claim 1, one or more polynucleotides of any of claims 2 to 3, one or more AAV vectors of claims 4 and 5, one or more cells of claim 6 and/or one or more pharmaceutical compositions according to claim 7, to the subject.

11. A kit comprising one or more ZFNs of claim 1, one or more polynucleotides of any of claims 2 to 3, one or more AAV vectors of claims 4 and 5, one or more cells of claim 6 and/or one or more pharmaceutical compositions according to claim 7.

12. A composition comprising:

(a) a first polynucleotide encoding a first ZFN designated 71557, the first polynucleotide optionally comprising an AAV vector comprising the sequences as shown in Table 4 or SEQ ID NO:43;

(b) a second polynucleotide encoding a second ZFN designated 71728, the second polynucleotide optionally comprising an AAV vector comprising the sequences as shown in Table 5 or SEQ ID NO:56; and

(c) a donor polynucleotide comprising a sequence encoding a Factor IX (FIX) sequence.

13. The composition of claim 12, wherein the donor polynucleotide is an AAV vector comprising the sequences as shown in Table 6, optionally the sequence as shown in SEQ ID NO:59.

14. The composition of claim 12 or 13, wherein the first, second and donor polynucleotides are carried on separate AAV vectors.

15. Use of the composition of any of claims 12 to 14 for expressing a FIX transgene in a subject in need thereof, wherein the composition is administered to the

subject such that the ZFN cleaves an endogenous albumin gene in the subject, the FIX sequence is integrated into the cleaved albumin gene and a FIX protein is expressed in the subject.

16. The use of claim 15, wherein a hemophilia is treated in the subject following expression of the FIX protein.

17. A method of expressing a FIX protein in a subject in need thereof, the method comprising administering one or more compositions of any of claims 12 to 14 to the subject such that that the FIX protein is expressed in the cell.

18. The method of claim 17, wherein the subject has a hemophilia and expression of the FIX protein treats and/or prevents the disease.

19. A kit comprising one or more compositions of any of claims 12-14.

20. A composition comprising:

(a) a first polynucleotide encoding a first ZFN designated 71557, the first polynucleotide optionally comprising an AAV vector comprising the sequences as shown in Table 4 or SEQ ID NO:43;

(b) a second polynucleotide encoding a second ZFN designated 71728, the second polynucleotide optionally comprising an AAV vector comprising the sequences as shown in Table 5 or SEQ ID NO:56; and

(c) a donor polynucleotide comprising a sequence encoding an iduronate-2-sulfatase (IDS) sequence.

21. The composition of claim 19, wherein the donor polynucleotide is an AAV vector comprising the sequences as shown in Table 7, optionally the sequence as shown in SEQ ID NO:65.

22. The composition of claim 20 or 21, wherein the first, second and donor polynucleotides are carried on separate AAV vectors.

23. Use of the composition of any of claims 20 to 22 for expressing an IDS transgene in a subject in need thereof, wherein the composition is administered to the subject such that the ZFN cleaves an endogenous albumin gene in the subject, the IDS sequence is integrated into the cleaved albumin gene and an IDS protein is expressed in the subject.

24. The use of claim 23, wherein MPS II is treated in the subject following expression of the IDS sequence.

25. A method of expressing an IDS protein in a subject in need thereof, the method comprising administering one or more compositions of any of claims 20 to 22 to the subject such that that the IDS protein is expressed in the cell.

26. The method of claim 25, wherein the subject has MPS II disease and expression of the IDS protein treats and/or prevents the disease.

27. A kit comprising one or more compositions of any of claims 20 to 22.

28. A composition comprising:

(a) a first polynucleotide encoding a first ZFN designated 71557, the first polynucleotide optionally comprising an AAV vector comprising the sequences as shown in Table 4 or SEQ ID NO:43;

(b) a second polynucleotide encoding a second ZFN designated 71728, the second polynucleotide optionally comprising an AAV vector comprising the sequences as shown in Table 5 or SEQ ID NO:56; and

(c) a donor polynucleotide comprising a sequence encoding an alpha-L iduronidase (IDUA) sequence.

29. The composition of claim 28, wherein the donor comprises the sequences as shown in Table 8, optionally the sequence as shown in SEQ ID NO:72.

30. The composition of claim 28 or claim 29, wherein the first, second and donor polynucleotides are carried on separate AAV vectors.

31. Use of the composition of any of claims 28 to 30, for expressing an IDUA transgene in a subject in need thereof, wherein the composition is administered to the subject such that the ZFN cleaves an endogenous albumin gene in the subject, the IDUA sequence is integrated into the cleaved albumin gene and an IDUA protein is expressed in the subject.

32. The use of claim 31, wherein MPS I is treated in the subject following expression of the IDUA sequence.

33. A method of expressing an IDUA protein in a subject in need thereof, the method comprising administering one or more compositions of any of claims 28 to 30 to the subject such that that the IDUA protein is expressed in the cell.

34. The method of claim 33, wherein the subject has MPS I disease and expression of the IDUA protein treats and/or prevents the disease.

35. A kit comprising one or more compositions of any of claims 28 to 30.