CLAIMS

1. Use of a recombinant human α-L-iduronidase (IDUA) produced by human neuronal cells in the manufacture of a medicament for treating a human subject diagnosed with mucopolysaccharidosis I (MPS I), wherein the medicament comprises a therapeutically effective amount of the recombinant human IDUA, and wherein the medicament is suitable for delivery to the cerebrospinal fluid of the brain of the human subject.

2. Use of a recombinant human IDUA produced by human glial cells in the manufacture of a medicament for treating a human subject diagnosed with MPS I, wherein the medicament comprises a therapeutically effective amount of the recombinant human IDUA, and wherein the medicament is suitable for delivery to the cerebrospinal fluid of the brain of the human subject.

3. The use of claim 1 or 2, wherein the medicament comprising the recombinant human IDUA is to be administered to the human subject after or concurrently with a medicament comprising an immune suppression therapy, and wherein the medicament comprising the immune suppression therapy is to continue to be administered to the human subject thereafter.

4. Use of a α2,6-sialylated human IDUA in the manufacture of a medicament for treating a human subject diagnosed with MPS I, wherein the medicament comprises a therapeutically effective amount of the α2,6-sialylated human IDUA, wherein the medicament is suitable for delivery to the cerebrospinal fluid of the brain of the human subject, the medicament comprising the α2,6-sialylated human IDUA is to be administered to the human subject after or concurrently with a medicament comprising an immune suppression therapy, and wherein the medicament comprising the immune suppression therapy is to continue to be administered to the human subject thereafter.

5. Use of a glycosylated human IDUA that does not contain detectable NeuGc in the manufacture of a medicament for treating a human subject diagnosed with MPS I, wherein the medicament comprises a therapeutically effective amount of the glycosylated human IDUA, wherein the medicament is suitable for delivery to the cerebrospinal fluid of the brain of the human subject, the medicament comprising the glycosylated human IDUA, is to be administered to the human subject after or concurrently with a medicament comprising an immune suppression

therapy and wherein the medicament comprising the immune suppression therapy is to continue to be administered to the human subject thereafter.

6. Use of a glycosylated human IDUA that does not contain detectable NeuGc and/or α-Gal antigen in the manufacture of a medicament for treating a human subject diagnosed with MPS I, wherein the medicament comprises a therapeutically effective amount of the glycosylated human IDUA, wherein the medicament is suitable for delivery to the cerebrospinal fluid of the brain of the human subject, the medicament comprising the glycosylated human IDUA is to be administered to the human subject after or concurrently with a medicament comprising an immune suppression therapy and wherein the medicament comprising the immune suppression therapy is to continue to be administered to the human subject thereafter.

7. Use of a human IDUA that contains tyrosine-sulfation in the manufacture of a medicament for treating a human subject diagnosed with MPS I, wherein the medicament comprises a therapeutically effective amount of the human IDUA, wherein the medicament is suitable for delivery to the cerebrospinal fluid of the brain of the human subject, the medicament comprising the human IDUA is to be administered to the human subject after or concurrently with a medicament comprising an immune suppression therapy, and wherein the medicament comprising the immune suppression therapy is to continue to be administered to the human subject thereafter.

8. Use of an expression vector encoding human IDUA in the manufacture of a medicament for treating a human subject diagnosed with MPS I, wherein the medicament is suitable for delivery to the brain of the human subject, wherein the IDUA is α2,6-sialylated upon expression from the expression vector in a human immortalized neuronal cell, the medicament comprising the expression vector is to be administered to the human subject after or concurrently with a medicament comprising an immune suppression therapy, and wherein the medicament comprising the immune suppression therapy is to continue to be administered to the human subject thereafter.

9. Use of an expression vector encoding human IDUA in the manufacture of a medicament for treating a human subject diagnosed with MPS I, wherein the medicament is suitable for delivery to the brain of the human subject, wherein the IDUA is glycosylated but does not contain detectable NeuGc upon expression from the expression vector in a human immortalized neuronal cell, the medicament comprising the expression vector is to be administered to the human subject after or

concurrently with a medicament comprising an immune suppression therapy, and wherein the medicament comprising the immune suppression therapy is to continue to be administered to the human subject thereafter.

10. Use of an expression vector encoding human IDUA in the manufacture of a medicament for treating a human subject diagnosed with MPS I, wherein the medicament is suitable for delivery to the brain of the human subject, wherein the IDUA is glycosylated but does not contain detectable NeuGc and/or α-Gal antigen upon expression from the expression vector in a human immortalized neuronal cell, the medicament comprising the expression vector is to be administered to the human subject after or concurrently with a medicament comprising an immune suppression therapy, and wherein the medicament comprising the immune suppression therapy is to continue to be administered to the human subject thereafter.

11. Use of an expression vector encoding human IDUA in the manufacture of a medicament for treating a human subject diagnosed with MPS I, wherein the medicament is suitable for delivery to the brain of the human subject, wherein the IDUA is tyrosine-sulfated upon expression from the expression vector in a human immortalized neuronal cell, the medicament comprising the expression vector is to be administered to the human subject after or concurrently with a medicament comprising an immune suppression therapy, and wherein the medicament comprising the immune suppression therapy is to continue to be administered to the human subject-thereafter.

12. Use of a recombinant nucleotide expression vector encoding human IDUA in the manufacture of a medicament for treating a human subject diagnosed with MPS I, wherein the medicament is suitable for delivery to the cerebrospinal fluid of the brain of the human subject, so that a depot is formed that releases IDUA containing a α2,6-sialylated glycan, the medicament comprising the expression vector is to be administered to the human subject after or concurrently with a medicament comprising an immune suppression therapy, and wherein the medicament comprising the immune suppression therapy is to continue to be administered to the human subject thereafter.

13. Use of a recombinant nucleotide expression vector encoding human IDUA in the manufacture of a medicament for treating a human subject diagnosed with MPS I, wherein the medicament is suitable for delivery to the cerebrospinal fluid of the brain of the human subject, so

that a depot is formed that releases glycosylated human IDUA that does not contain detectable NeuGc, the medicament comprising the expression vector is to be administered to the human subject after or concurrently with a medicament comprising an immune suppression therapy, and wherein the medicament comprising the immune suppression therapy is to continue to be administered to the human subject thereafter.

14. Use of a recombinant nucleotide expression vector encoding human IDUA in the manufacture of a medicament for treating a human subject diagnosed with MPS I, wherein the medicament is suitable for delivery to the cerebrospinal fluid of the brain of the human subject, so that a depot is formed that releases glycosylated human IDUA that does not contain detectable NeuGc and/or α-Gal antigen, the medicament comprising the expression vector is to be administered to the human subject after or concurrently with a medicament comprising an immune suppression therapy, and wherein the medicament comprising the immune suppression therapy is to continue be administered to the human subject thereafter.

15. Use of a recombinant nucleotide expression vector encoding human IDUA in the manufacture of a medicament for treating a human subject diagnosed with MPS I, wherein the medicament is suitable for delivery to the cerebrospinal fluid of the brain of the human subject, so that a depot is formed that releases IDUA containing a tyrosine-sulfation, the medicament comprising the expression vector is to be administered after or concurrently with a medicament comprising an immune suppression therapy, and wherein the medicament comprising the immune suppression therapy is to continue to be administered to the human subject thereafter.

16. The use of any one of claims 3 to 15, wherein the immune suppression therapy comprises a combination of (a) tacrolimus and mycophenolic acid, (b) rapamycin and mycophenolic acid, or (c) tacrolimus, rapamycin, and a corticosteroid such as prednisolone and/or methylprednisolone.

17. The use of claim 16, wherein the immune suppression therapy is withdrawn after 180 days.

18. The use of any one of claims 1 to 17, wherein the human IDUA comprises the amino acid sequence of SEQ ID NO. 1.

19. The use of claim 18 wherein the immune suppression therapy comprises a combination of (a) tacrolimus and mycophenolic acid, (b) rapamycin and mycophenolic acid, or (c) tacrolimus, rapamycin, and a corticosteroid such as prednisolone and/or methylprednisolone.

20. The use of claim 19, wherein the medicament comprising the immune suppression therapy is withdrawn after 180 days.

21. The use of claim 12, wherein production of the IDUA containing a α2,6-sialylated glycan is confirmed by transducing a human neuronal cell line with the recombinant nucleotide expression vector in cell culture.

22. The use of claim 13, wherein production of the glycosylated IDUA that does not contain detectable NeuGc is confirmed by transducing a human neuronal cell line with the recombinant nucleotide expression vector in cell culture.

23. The use of claim 14, wherein production of the glycosylated IDUA that does not contain detectable NeuGc and/or α-Gal antigen is confirmed by transducing a human neuronal cell line with the recombinant nucleotide expression vector in cell culture.

24. The use of claim 15, wherein production of the IDUA containing a tyrosine-sulfation is confirmed by transducing a human neuronal cell line with the recombinant nucleotide expression vector in cell culture.

25. The use of any one of claims 21-24, wherein production is confirmed in the presence and absence of mannose-6-phosphate.

26. The use of any one of claims 8-17 and 21-25, wherein the expression vector or recombinant nucleotide expression vector encodes a signal peptide.

27. Use of a recombinant nucleotide expression vector encoding human IDUA in the manufacture of a medicament for treating a human subject diagnosed with MPS I, wherein the medicament is suitable for delivery to the cerebrospinal fluid of the brain of the human subject, so that a depot is formed that releases IDUA containing a α2,6-sialylated glycan, the medicament comprising the expression vector is to be administered to the human subject after or concurrently with a medicament comprising an immune suppression therapy, and wherein the medicament

comprising the immune suppression therapy is to continue to be administered to the human subject thereafter; and wherein the expression vector, when used to transduce human neuronal cells in culture results in production of the IDUA containing the α2,6-sialylated glycan in the culture.

28. Use of a recombinant nucleotide expression vector encoding human IDUA in the manufacture of a medicament for treating a human subject diagnosed with MPS I, wherein the medicament is suitable for delivery to the cerebrospinal fluid of the brain of the human subject, so that a depot is formed that releases glycosylated IDUA that does not contain detectable NeuGc, the medicament comprising the expression vector is to be administered to the human subject after or concurrently with a medicament comprising an immune suppression therapy, and wherein the medicament comprising the immune suppression therapy is to continue to be administered to the human subject thereafter; and wherein the expression vector, when used to transduce human neuronal cells in culture results in production of the IDUA that is glycosylated but does not contain detectable NeuGc in the culture.

29. Use of a recombinant nucleotide expression vector encoding human IDUA in the manufacture of a medicament for treating a human subject diagnosed with MPS I, wherein the medicament is suitable for delivery to the cerebrospinal fluid of the brain of the human subject, so that a depot is formed that releases glycosylated IDUA that does not contain detectable NeuGc and/or α-Gal antigen, the medicament comprising the expression vector is to be administered to the human subject after or concurrently with a medicament comprising an immune suppression therapy, and wherein the medicament comprising the immune suppression therapy is to continue to be administered to the human subject thereafter; and wherein the expression vector, when used to transduce human neuronal cells in culture results in production of the IDUA that is glycosylated but does not contain detectable NeuGc and/or α-Gal antigen in the culture.

30. Use of a recombinant nucleotide expression vector encoding human IDUA in the manufacture of a medicament for treating a human subject diagnosed with MPS I, wherein the medicament is suitable for delivery to the cerebrospinal fluid of the brain of the human subject, so that a depot is formed that releases IDUA that contains a tyrosine-sulfation, the medicament comprising the expression vector is to be administered to the human subject after or concurrently with a medicament comprising an immune suppression therapy, and wherein the medicament

comprising the immune suppression therapy is to continue to be administered to the human subject thereafter; and wherein the expression vector, when used to transduce human neuronal cells in culture results in production of the IDUA that is tyrosine-sulfated in the culture.

31. The use of any of claims 27 to 30, wherein the immune suppression therapy comprises a combination of (a) tacrolimus and mycophenolic acid, (b) rapamycin and mycophenolic acid, or (c) tacrolimus, rapamycin, and a corticosteroid such as prednisolone and/or methylprednisolone.

32. The use of claim 31, wherein the medicament comprising the immune suppression therapy is withdrawn after 180 days.

33. The use of any one of claims 1-32, wherein the human subject is younger than 3 years of age.

34. The use of any one of claims 8-33, wherein the human subject is younger than 3 years of age and the medicament comprising the expression vector or the recombinant nucleotide expression vector is suitable for delivery at a dose of 2×10^9 GC/g brain mass, 1×10^{10} GC/g brain mass, or 5×10^{10} GC/g brain mass.

35. The use of any one of claims 8-33, wherein the human subject is younger than 3 years of age and the medicament comprising the expression vector or the recombinant nucleotide expression vector is suitable for delivery at a dose ranging from 2×10^9 GC/g brain mass to 1×10^{10} GC/g brain mass.

36. The use of any one of claims 8-33, wherein the human subject is younger than 3 years of age and the medicament comprising the expression vector or the recombinant nucleotide expression vector is suitable for delivery at a dose ranging from 1×10^{10} GC/g brain mass to 5×10^{10} GC/g brain mass.