

CLAIMS

What is claimed:

1. A method of treating muscular dystrophy comprising administering a therapeutically effective amount of recombinant AAV vector comprising 1) a nucleic acid sequence that is at least 85% identical to the nucleic acid sequence of SEQ ID NO:1, 2) a nucleotide that hybridizes under stringent condition to the nucleotide sequence of SEQ ID NO: 1 or 3) a fragment of nucleic acid of SEQ ID NO: 1 encoding a protein that exhibits ANO5 activity to a subject in need thereof.
2. A method of regenerating muscle in a subject in need comprising administering a recombinant AAV vector comprising 1) a nucleic acid sequence that is at least 85% identical to the nucleic acid sequence of SEQ ID NO:1, 2) a nucleotide that hybridizes under stringent condition to the nucleotide sequence of SEQ ID NO: 1, or 3) a fragment of nucleic acid of SEQ ID NO: 1 encoding a protein that exhibits ANO5 activity to the subject in an amount effective to regenerate muscle.
3. A method of treating chronic muscle wasting comprising administering a therapeutically effective amount of recombinant AAV vector comprising 1) a nucleic acid sequence is at least 85% identical to the SEQ ID NO:1, 2) a nucleotide that hybridizes under stringent condition to the nucleotide sequence of SEQ ID NO: 1 or 3) a fragment of nucleic acid of SEQ ID NO: 1 encoding a protein that exhibits ANO5 activity to a subject in need thereof.
4. The method of any one of claims 1-3 wherein the recombinant AAV comprises a polynucleotide sequence of SEQ ID NO: 1.
5. The method of any one of claims 1-4 wherein the recombinant AAV vector of is AAV1, AAV2, AAV4, AAV5, AAV6, AAV7, AAV8, AAV9, AAV10, AAV11, AAV12, AAV13 or AAV rh.74.
6. The method of any one of claims 1-5 wherein the recombinant AAV vector comprises a polynucleotide operably linked to a muscle-specific control element.
7. The method of claim 6 wherein the muscle-specific control element is human skeletal actin gene element, cardiac actin gene element, myocyte-specific enhancer

binding factor MEF, murine creatine kinase enhancer element, skeletal fast-twitch troponin C gene element, slow-twitch cardiac troponin C gene element, the slow-twitch troponin I gene element, hypoxia-inducible nuclear factors, steroid-inducible element or glucocorticoid response element (GRE).

- 5 8. The method of any one of claims 2-7 wherein the subject is suffering from muscular dystrophy.
9. The method of any one of claims 1-8 wherein the muscular dystrophy is dysferlin-associated muscular dystrophy, limb girdle muscular dystrophy type 2L, or Miyoshi myopathy type 3, Bethlem myopathy, calpainopathy, desmin myopathy,
- 10 10. The method of any one of claims 1-9 wherein the subject has a recessive mutation in the ANO5 gene.
11. The method of any one of claims 1-10 wherein the recombinant AAV vector is
- 15 12. The method of any one of claims 1-11 further comprising the step of administering a therapeutically effective amount of an antioxidant composition to a subject in need thereof.
13. The method of claim 12 wherein the antioxidant composition comprises at
- 20 14. The method of claim 12 or 13 wherein the antioxidant composition comprises coenzyme Q10, lipoic acid, vitamin, carotenoid, vitamin cofactor, mineral, polyphenol, or flavonoid.
15. A method of treating muscular dystrophy comprising administering a
- 25 16. The method of any one of claims 1-15 wherein the subject is suffering from a muscular dystrophy associated with a mutation in the ANO5 gene.

16. A method of treating chronic muscle wasting comprising administering a therapeutically effective amount of an antioxidant composition, to a subject in need thereof.
17. A method of slowing the progression of muscular dystrophy comprising
5 administering a therapeutically effective amount of an antioxidant composition, to a subject in need thereof.
18. A method of slowing the progression of chronic muscle wasting comprising administering a therapeutically effective amount of an antioxidant composition to a subject in need thereof.
- 10 19. The method of any one of claims 15-18 wherein the antioxidant composition comprises at least one of a coenzyme Q10, lipoic acid, vitamin, carotenoid, vitamin cofactor, mineral, polyphenol, or flavonoid.
20. The method of any one of claims 15-19 wherein the antioxidant composition comprises coenzyme Q10, lipoic acid and vitamin E.
- 15 21. The method of any one of claims 15-20 wherein muscular dystrophy is dysferlin-associated muscular dystrophy, limb girdle muscular dystrophy type 2L, or Miyoshi myopathy type 3, Bethlem myopathy, calpainopathy, desmin myopathy, dysferlinopathy, myofibrillar myopathy, sarcoglycanopathie or ZASP-related myopathy.
- 20 22. The method of any one of claims 15-21 wherein the oxidative stress is reduced in skeletal muscle of the subject.
23. The method of any one of claims 15-21 wherein the skeletal muscle function of the subject is improved.
24. The method of any one of claims 15-21 wherein the subject has a recessive
25 mutation in the ANO5 gene.
25. The method of any one of claims 12-25 wherein the antioxidant composition is administered orally.

26. The method of any one of claims 12-25 wherein the antioxidants are in the same composition.
27. The method of any one of claims 12-25 wherein the antioxidants are in separate compositions.
- 5 28. The methods of any one of claims 12-25 wherein the antioxidants of the antioxidant composition are administered concurrently.
29. The method of any one of claims 12-25 wherein the antioxidants of the antioxidant composition are administered at separate times or consecutively.
30. The method of any one of claims 12-29 wherein the antioxidant composition
10 is administered once daily, once weekly, twice weekly, once every two weeks, once every three weeks, monthly or once every two months.
31. A composition comprising a therapeutically effective amount of a recombinant AAV vector comprising 1) a nucleic acid sequence is at least 85% identical to the nucleic acid sequence of SEQ ID NO:1, 2) a nucleotide that hybridizes under stringent
15 condition to the nucleotide sequence of SEQ ID NO: 1 or 3) a fragment of nucleic acid of SEQ ID NO: 1 encoding a protein that exhibits ANO5 activity, for the treatment of muscular dystrophy in a subject in need.
32. A composition comprising a recombinant AAV vector comprising 1) a nucleic acid sequence is at least 85% identical to the SEQ ID NO:1, 2) a nucleotide that
20 hybridizes under stringent condition to the nucleotide sequence of SEQ ID NO: 1 or 3) a fragment of nucleic acid of SEQ ID NO: 1 encoding a protein that exhibits ANO5 activity to a subject in need thereof, for the regeneration of muscle in a subject in need.
33. A composition comprising a therapeutically effective amount of a recombinant
25 AAV vector comprising 1) a nucleic acid sequence is at least 85% identical to the nucleic acid sequence of SEQ ID NO:1, 2) a nucleotide that hybridizes under stringent condition to the nucleotide sequence of SEQ ID NO: 1, or 3) a fragment of nucleic acid of SEQ ID NO: 1 encoding a protein that exhibits ANO5 activity for the treatment of chronic muscle wasting in a subject in need.

34. The composition of any one of claims 31-33 wherein the recombinant AAV comprises a polynucleotide sequence of SEQ ID NO: 1.
35. The composition of any one of claims 31-34, wherein the recombinant AAV vector of is AAV1, AAV2, AAV4, AAV5, AAV6, AAV7, AAV8, AAV9, AAV10,
5 AAV11, AAV12, AAV13 or AAV rh.74.
36. The composition of any one of claims 31-35 wherein the recombinant AAV vector comprises a polynucleotide operably linked to a muscle-specific control element.
37. The composition of claim 36 wherein the muscle-specific control element is
10 human skeletal actin gene element, cardiac actin gene element, myocyte-specific enhancer binding factor MEF, murine creatine kinase enhancer element, skeletal fast-twitch troponin C gene element, slow-twitch cardiac troponin C gene element, the slow-twitch troponin I gene element, hypoxia-inducible nuclear factors, steroid-inducible element or glucocorticoid response element (GRE).
- 15 38. The composition of any one of claims 31-37 wherein the subject is suffering from muscular dystrophy.
39. The composition of any one of claims 31-39 wherein the muscular dystrophy is dysferlin-associated muscular dystrophy, limb girdle muscular dystrophy type 2L, Miyoshi myopathy type 3, Bethlem myopathy, calpainopathy, desmin myopathy,
20 dysferlinopathy, myofibrillar myopathy, sarcoglycanopathy or ZASP-related myopathy.
40. The composition of any one of claims 31-39 wherein the subject has a recessive mutation in the ANO5 gene.
41. The composition of any one of claims 31-40 that is formulated for
25 intramuscular or intravenous injection.
42. The composition of any one of claims 31-41 further comprising a therapeutically effective amount of an antioxidant composition.

43. The composition of claim 42, wherein the antioxidant composition comprises at least one of coenzyme Q10, lipoic acid, vitamin, carotenoid, vitamin cofactor, mineral, polyphenol, or flavonoid,
44. The composition of claim 42 or 43, wherein the antioxidant composition
5 comprises coenzyme Q10, lipoic acid and vitamin E.
45. A composition comprising a therapeutically effective amount of an antioxidant composition, for the treatment of muscular dystrophy in a subject in need.
46. A composition comprising a therapeutically effective amount of an antioxidant composition, for the treatment of chronic muscle wasting in a subject in need.
- 10 47. A composition comprising a therapeutically effective amount of an antioxidant composition, for slowing the progression of muscular dystrophy in a subject in need.
48. A composition comprising a therapeutically effective amount of an antioxidant composition, for slowing the progression of chronic muscle wasting in a subject in need.
- 15 49. The composition of any one of claims 45-48 wherein the antioxidant composition comprises at least one of coenzyme Q10, lipoic acid, vitamin, carotenoid, vitamin cofactor, mineral, polyphenol, or flavonoid,
50. The composition of any one of claims 45-49. wherein the antioxidant composition comprises coenzyme Q10, lipoic acid and vitamin E.
- 20 51. The composition of any one of claims 45-50 wherein muscular dystrophy is dysferlin-associated muscular dystrophy, limb girdle muscular dystrophy type 2L, or Miyoshi myopathy type 3, Bethlem myopathy, calpainopathy, desmin myopathy, dysferlinopathy, myofibrillar myopathy, sarcoglycanopathie or ZASP-related myopathy.
- 25 52. The composition of any one of claims 45-51 wherein oxidative stress is reduced in skeletal muscle of the subject.

53. The composition of any one of claims 45-51 wherein skeletal muscle function of the subject is improved.
54. The composition of any one of claims 45-51 wherein the subject has a recessive mutation in the ANO5 gene.
- 5 55. The composition of any one of claims 42-54 that is formulated for oral administration.
56. The composition of any one of claims 42-55 wherein the agents are in the same composition.
57. The composition of any one of claims 42-55 wherein the agents are in
10 separate compositions.
58. The composition of any one of claims 42-55 wherein the antioxidants of the antioxidant composition are administered concurrently.
59. The composition of any one of claims 42-55 wherein the antioxidants of the antioxidant composition are administered at separate times or consecutively.
- 15 60. The composition of any one of claims 45-59 wherein the antioxidant composition is administered once daily, once weekly, twice weekly, once every two weeks, once every three weeks, monthly or once every two months.
61. Use of a recombinant AAV vector comprising 1) a nucleic acid sequence is at least 85% identical to the nucleic acid sequence of SEQ ID NO:1, 2) a nucleotide that
20 hybridizes under stringent condition to the nucleotide sequence of SEQ ID NO: 1 or 3) a fragment of nucleic acid of SEQ ID NO: 1 encoding a protein that exhibits ANO5 activity for the preparation of a medicament for treatment of muscular dystrophy in a subject in need thereof.
62. Use of a recombinant AAV vector comprising 1) a nucleic acid sequence is at
25 least 85% identical to the nucleic acid sequence of SEQ ID NO:1, 2) a nucleotide that hybridizes under stringent condition to the nucleotide sequence of SEQ ID NO: 1, or 3) a fragment of nucleic acid of SEQ ID NO: 1 encoding a protein that exhibits ANO5

activity to a subject in need thereof for the preparation of a medicament for regenerating muscle in subject in need thereof.

63. Use of a recombinant AAV vector comprising 1) a nucleic acid sequence is at least 85% identical to the nucleic acid sequence of SEQ ID NO:1, 2) a nucleotide that
5 hybridizes under stringent condition to the nucleotide sequence of SEQ ID NO: 1, or
3) a fragment of nucleic acid of SEQ ID NO: 1 encoding a protein that exhibits ANO5 activity for the preparation of a medicament for the treatment of chronic muscle wasting syndrome.
64. The use of any one of claims 61-63 wherein the recombinant AAV comprises
10 a polynucleotide sequence of SEQ ID NO: 1.
65. The use of any one of claims 61-63 wherein the recombinant AAV vector of is AAV1, AAV2, AAV4, AAV5, AAV6, AAV7, AAV8, AAV9, AAV10, AAV11, AAV12, AAV13 or AAV rh.74.
66. The use of any one of claims 61-65 wherein the recombinant AAV vector
15 comprises a polynucleotide operably linked to a muscle-specific control element.
67. The use of claim 66 wherein the muscle-specific control element is human skeletal actin gene element, cardiac actin gene element, myocyte-specific enhancer binding factor MEF, murine creatine kinase enhancer element, skeletal fast-twitch troponin C gene element, slow-twitch cardiac troponin C gene element, the slow-
20 twitch troponin I gene element, hypozia-inducible nuclear factors, steroid-inducible element or glucocorticoid response element (GRE).
68. The use of claims 61-67 wherein the subject is suffering from muscular dystrophy.
69. The use of any one of claims 61-68 wherein the subject is suffering from
25 dysferlin-associated muscular dystrophy, limb girdle muscular dystrophy type 2L, Miyoshi myopathy type 3, Bethlem myopathy, calpainopathy, desmin myopathy, dysferlinopathy, myofibrillar myopathy, sarcoglycanopathie or ZASP-related myopathy.

70. The use of any one of claims 61-69 wherein the subject has a recessive mutation in the ANO5 gene.
71. The use of any one of claims 61-70 wherein the medicament is formulated for intramuscular or intravenous injection.
- 5 72. The use of any one of claims 61-71 further comprising a therapeutically effective amount of an antioxidant composition, to a subject in need thereof.
73. The use of claim 72, wherein the antioxidant composition comprises at least one of coenzyme Q10, lipoic acid, vitamin, carotenoid, vitamin cofactor, mineral, polyphenol, or flavonoid,
- 10 74. The use of claim 72 or 73, wherein the antioxidant composition comprises coenzyme Q10, lipoic acid and vitamin E.
75. Use of a therapeutically effective amount of an antioxidant composition, for the preparation of a medicament for the treatment of muscular dystrophy in a subject in need.
- 15 76. Use of a therapeutically effective amount of an antioxidant composition, , for the preparation of a medicament for the treatment of chronic muscle wasting syndrome.
77. Use of a therapeutically effective amount of an antioxidant composition, for the preparation of a medicament for slowing the progression of muscular dystrophy in
20 a subject in need.
78. Use of a therapeutically effective amount of an antioxidant composition, for the preparation of a medicament for slowing the progression of chronic muscle wasting syndrome in a subject in need.
79. The use of any one of claims 75-78, wherein the antioxidant composition
25 comprises at least one of coenzyme Q10, lipoic acid, vitamin, carotenoid, vitamin cofactor, mineral, polyphenol, or flavonoid,

80. The method of any one of claims 75-79. wherein the antioxidant composition comprises coenzyme Q10, lipoic acid and vitamin E.
81. The use of any one of claims 75-80 wherein the subject is suffering from dysferlin-associated muscular dystrophy, limb girdle muscular dystrophy type 2L, or
5 Miyoshi myopathy type 3, Bethlem myopathy, calpainopathy, desmin myopathy, dysferlinopathy, myofibrillar myopathy, sarcoglycanopathy or ZASP-related myopathy.
82. The use of any one of claims 75-81 wherein oxidative stress is reduced in skeletal muscle of the subject.
- 10 83. The use of any one of claims 75-81 wherein skeletal muscle function of the subject is improved.
84. The use of any one of claims 75-81 wherein the subject has a recessive mutation in the ANO5 gene.
85. The use of any one of claims 55-84 wherein the medicament is formulated for
15 oral administration.
86. A method of any of claims 15-30 further comprising administering a therapeutically effective amount of recombinant AAV vector comprising 1) a nucleic acid sequence that is at least 85% identical to the nucleic acid sequence of SEQ ID NO:1, 2) a nucleotide that hybridizes under stringent condition to the nucleotide
20 sequence of SEQ ID NO:1 or 3) a fragment of nucleic acid of SEQ ID NO:1 encoding a protein that exhibits ANO5 activity, in combination with a therapeutically effective amount of an antioxidant composition, to a subject in need thereof.
87. The method of claim 86, wherein the antioxidant composition comprises at least one of coenzyme Q10, lipoic acid, vitamin, carotenoid, vitamin cofactor,
25 mineral, polyphenol, or flavonoid,
88. The method of claim 86 or 87, wherein the antioxidant composition comprises coenzyme Q10, lipoic acid and vitamin E.

89. A method of any one of claims 86-88, wherein the recombinant AAV vector comprises a polynucleotide sequence of SEQ ID NO:1.
90. A method of any one of claims 86-89 wherein the recombinant AAV vector is AAV1, AAV2, AAV4, AAV5, AAV6, AAV7, AAV8, AAV9, AAV10, AAV11,
5 AAV12, AAV13 or AAV rh.74.
91. A method of any one of claims 86-89 wherein the recombinant AAV vector is administered by intramuscular or intravenous injection.
92. A method of any one of claims 86-91 wherein the antioxidant composition is administered orally.
- 10 93. The method of any one of claims 86-91, wherein the said recombinant AAV vector and antioxidant composition are in the same composition.
94. The method of any one of claims 86-92, wherein the said recombinant AAV vector and antioxidant composition are in separate compositions.
95. The method of any one of claims 86-92, wherein the said recombinant AAV
15 vector and antioxidant composition are administered concurrently.
96. The method of any one of claims 86-92 wherein the said recombinant AAV vector and antioxidant composition are administered at separate times or consecutively.
97. The method of any one of claims 86-96 wherein the said recombinant AAV
20 vector and antioxidant composition are administered once daily, once weekly, twice weekly, once every two weeks, once every three weeks, monthly or once every two months.