CLAIMS

1. A nucleic acid construct comprising a nucleotide sequence encoding a lamin A polypeptide and a lamin C polypeptide, or a biologically active variant and/or fragment thereof, wherein said construct comprises at least intron 8 or intron 11 of the wildtype-human *LMNA* gene.

2. The nucleic acid construct of claim 1, wherein intron 8 comprises a nucleotide sequence that is at least 80%, 85%, 90%, 95%, 98%, 99% or 100% identical to the nucleotide sequence of SEQ ID NO: 77, or a fragment thereof.

3. The nucleic acid construct of claim 1, wherein intron 11 comprises a nucleotide sequence that is at least 80%, 85%, 90%, 95%, 98%, 99% or 100% identical to the nucleotide sequence of SEQ ID NO: 80, or a fragment thereof.

4. The nucleic acid construct of any one of claims 1-3, wherein the nucleotide sequence comprises introns 8 and 11 of the wildtype-human *LMNA* gene.

5. The nucleic acid construct of any one of claims 1-4, wherein the nucleotide sequence further comprises introns 9 and 10 of the wildtype-human *LMNA* gene.

6. The nucleic acid construct of any one of claims 1-5, wherein the nucleic acid construct lacks introns 1-7 of the wildtype human *LMNA* gene.

7. The nucleic acid construct of any one of claims 1-6, wherein the nucleic acid construct comprises introns 8-11 of the wildtype human *LMNA* gene, and lacks introns 1-7 of the wildtype human *LMNA* gene.

8. The nucleic acid construct of any one of claims 1-7, wherein the nucleic acid construct further comprises a regulatory element and wherein the regulatory element has less than or equal to 800 base pairs (bp), 700 bp, 600 bp, 500 bp, 400 bp, 300 bp, 250 bp, 200 bp, 150 bp, 140 bp, 130 bp, 120 bp, 110 bp, 100 bp, 70 bp, or 50 bp.

9. The nucleic acid construct of any one of claims 1-8, wherein the nucleic acid construct further comprises a regulatory element and wherein the regulatory element is any one of or combination of: any one of SEQ ID NOs: 30-58, SEQ ID NO: 102, CBA, CMV, SCP, SERpE_TTR, Proto1, minCMV, UCL-HLP, CMVe, Myh6, Desmin, cTnT, α-MHC, MLC-2, CAG, or EFS.

10. The nucleic acid construct of claim 8 or 9, wherein the regulatory element is cell-type selective.

11. The nucleic acid construct of claim 10, wherein the regulatory element is selectively expressed in cardiomyocytes.

12. The nucleic acid construct of claim 11, wherein the regulatory element is any one of or combination of Myh6, Desmin, cTnT, α-MHC, or MLC-2.

13. The nucleic acid construct of claim 10, wherein the regulatory element is cTNT.

14. The nucleic acid construct of claim 13, wherein the cTNT regulatory element comprises SEQ ID NO: 101.

15. The nucleic acid construct of any one of claims 1-14, wherein the nucleic acid construct comprises a nucleotide sequence that is at least 80%, 90%, 95%, or 100% identical to the nucleotide sequence of SEQ ID NO: 3 or SEQ ID NO: 8, or a codon-optimized variant and/or a fragment thereof.

16. The nucleic acid construct of any one of claims 1-15, wherein the nucleotide sequence encodes a lamin A polypeptide comprising an amino acid sequence that is at least 80%, 85%, 90%, 95%, 98%, 99% or 100% identical to the amino acid sequence of SEQ ID NO: 12, or a biologically active fragment thereof, and a lamin C polypeptide comprising an amino acid sequence that is at least 80%, 85%, 90%, 95%, 98%, 99% or 100% identical to the amino acid sequence of SEQ ID NO: 13, or a biologically active fragment thereof.

16. The nucleic acid construct of any one of claims 1-15, wherein the nucleotide sequence encodes a lamin A polypeptide comprising an amino acid sequence that is at least 80%, 85%, 90%, 95%, 98%, 99% or 100% identical to the amino acid sequence of SEQ ID NO: 21, or a biologically active fragment thereof, and a lamin C polypeptide comprising an amino acid sequence that is at least 80%, 85%, 90%, 95%, 98%, 99% or 100% identical to the amino acid sequence of SEQ ID NO: 13, or a biologically active fragment thereof.

17. The nucleic acid construct of any one of claims 1-16, wherein the nucleotide sequence further comprises a polyadenylation signal.

18. A viral vector comprising the nucleic acid construct of any one of claims 1-17.

19. The viral vector of claim 18, wherein the viral vector is an adeno-associated virus (AAV) vector.

20. The viral vector of claim 19, wherein the AAV vector is AAV1, AAV2, AAV5, AAV6, AAV8, AAV9, scAAV1, scAAV2, scAAV5, scAAV6, scAAV8, or scAAV9.

21. The viral vector of claim 19 or 20, wherein the nucleotide sequence further comprises a 5' AAV inverted terminal repeat (ITR) sequence and a 3' AAV ITR sequence.

22. A viral particle comprising the viral vector of any one of claims 18-21.

23. The viral particle of claim 22, wherein the viral particle comprises capsid proteins of an AAV.

24. The viral particle of any one of claims 19-23, wherein the AAV is an AAV6 or AAV9.

25. A host cell comprising the nucleic acid construct of any one of claims 1-16, the viral vector of any one of claims 18-21, or the viral particle of any one of claims 22-24.

26. A pharmaceutical composition comprising the nucleic acid construct of any one of claims 1-16, the viral vector of any one of claims 18-21, the viral particle of any one of claims 22-24, or the host cell of claim 25, and one or more pharmaceutically acceptable excipients.

27. Use of a therapeutically effective amount of the nucleic acid construct of any one of claims 1-17, the viral vector of any one of claims 18-21, the viral particle of any one of claims 22-24, the host cell of claim 25, or the pharmaceutical composition of claim 26 in the manufacture of a medicament for treating a laminopathy in a subject in need thereof.

28 Use of a therapeutically effective amount of the nucleic acid construct of any one of claims 1-16, the viral vector of any one of claims 18-21, the viral particle of any one of claims 22-24, the host cell of claim 25, or the pharmaceutical composition of claim 26 in the manufacture of a medicament for expressing a lamin A polypeptide and a lamin C polypeptide, or a biologically active variant and/or a fragment thereof in a subject.

29. Use of a therapeutically effective amount of the nucleic acid construct of any one of claims 1-16, the viral vector of any one of claims 18-21, the viral particle of any one of claims 22-24, the host cell of claim 25, or the pharmaceutical composition of claim 26 in the manufacture of a

medicament for increasing expression of a functional lamin A polypeptide and a functional lamin C polypeptide, or a biologically active variant and/or a fragment thereof in a subject.

30. The use of claim 28 or 29, wherein the subject is suffering from a laminopathy.

31. The use of claim 27 or 30, wherein the laminopathy is any one or more of: Charcot-Marie-Tooth disease, Emery-Dreifuss muscular dystrophy, familial partial lipodystrophy, Hutchinson-Gilford progeria syndrome, limb-girdle muscular dystrophy, *LMNA*-related congenital muscular dystrophy, mandibuloacral dysplasia, arrhythmogenic right ventricular cardiomyopathy, familial atrial fibrillation, left ventricular noncompaction, or dilated cardiomyopathy.

32. The use of any one of claims 27-31, wherein said nucleic acid construct, viral vector, viral particle, host cell, or pharmaceutical composition is to be administered intramyocardially, intravenously, intramuscularly, intrathecally, subcutaneously, systemically, or locally into the myocardium.