CLAIMS

WHAT IS CLAIMED IS:

1. Use of a composition comprising (a) a viral vector comprising a nucleic acid sequence that is at least 90% identical to SEQ ID NO: 2 encoding a plakophilin 2 (PKP2) polypeptide operatively linked to a cardiac specific promoter and a 3' element; and (b) a pharmaceutically acceptable carrier or excipient in the manufacture of a medicament for treating arrhythmogenic right ventricular cardiomyopathy (ARVC) or arrhythmogenic cardiomyopathy (ACM) in a mammal with ARVC or ACM.

2. The use of claim 1, wherein the viral vector is selected from the group consisting of an adeno-associated virus, an adenovirus, a lentivirus, a pox virus, a vaccinia virus, and a herpes virus.

3. The use of claim 1, wherein the viral vector is an adeno-associated virus.

4. The use of claim 3, wherein the adeno-associated virus is selected from the group consisting of an AAV6, an AAV.rh74, an AAV8, and an AAV9.

5. The use of claim 4, wherein the adeno-associated virus is an AAV9.

6. The use of claim 1, wherein the viral vector further comprises a cardiac specific enhancer.

7. The use of claim 1, wherein the 3' element comprises a Woodchuck Hepatitis Virus Posttranscriptional Regulatory Element (WPRE), a bovine growth hormone polyadenylation (bGH polyA) sequence, or a combination thereof.

8. The use of claim 1, wherein the nucleic acid encoding the PKP2 gene is at least 95% identical to SEQ ID NO: 2.

9. The use of claim 1, wherein the nucleic acid encoding the PKP2 gene is identical to SEQ ID NO: 2.

10. The use of claim 1, wherein the PKP2 gene encodes a PKP2 polypeptide having a sequence of SEQ ID NO: 8.

11. The use of claim 1, wherein the pharmaceutically acceptable carrier or excipient comprises a buffer, a polymer, a salt, or a combination thereof.

12. The use of claim 1, wherein the medicament reverses, reduces, or prevents at least one of fibrofatty tissue replacement; myocardial atrophy; predominant right ventricular dilation; ventricular arrhythmias; sudden cardiac death; exercise-triggered cardiac events; right ventricular cardiomyopathy, dilation, or heart failure; left ventricular cardiomyopathy, dilation, or heart failure; atrial arrhythmias; syncope; palpitations; shortness of breath; or chest pain.

13. The use of claim 1, wherein the medicament restores desmosome structure and/or function.

14. The use of claim 1, wherein the medicament restores PKP2 protein and activity levels.

15. The use of claim 1, wherein the medicament restores PKP2 induced gene expression.

16. The use of claim 1, wherein the medicament restores expression of one or more of Ryanodine Receptor 2 (Ryr2), Ankyrin-B (Ank2), Cacna1c (CaV1.2), Triadin (Trdn), or Calsequestrin-2 (Casq2).

17. The use of claim 1, wherein the mammal is identified as having at least one variation in a desmosome protein.

18. The use of claim 17, wherein the desmosome protein is PKP2.

19. The use of claim 18, wherein the variation comprises a deletion, an insertion, a single nucleotide variation, or a copy number variation.