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(54) Title: OPTIMIZED EXPRESSION CASSETTES FOR GENE THERAPY

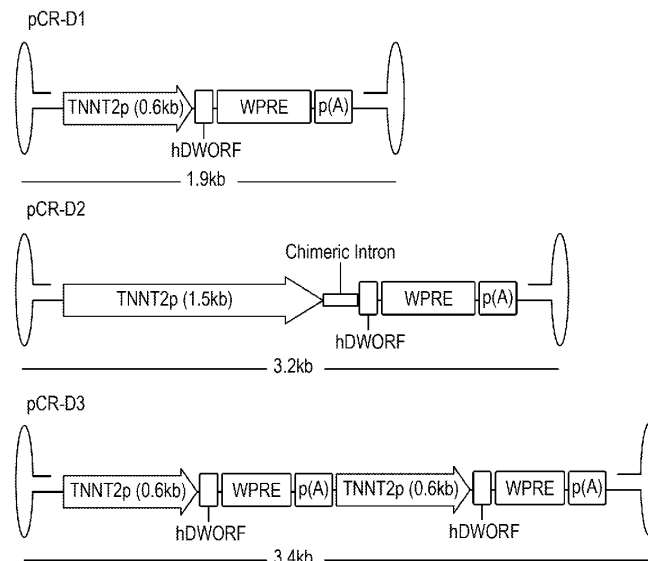


FIG. 1

(57) **Abstract:** In some aspects, cardiac-specific expression cassettes are provided herein. In some aspects, provided herein is an expression cassette comprising a polynucleotide sequence encoding a gene product for therapy of a heart disease, wherein the polynucleotide sequence is operably linked to promoter (e.g., a cardiac-specific promoter), and optionally an enhancer (e.g., a cardiac-specific enhancer). In some aspects, the disclosure provides recombinant adeno-associated virus (rAAV) virions, comprising a capsid protein and a viral genome comprising an expression cassette comprising a polynucleotide sequence encoding a therapeutic gene product, e.g., dwarf open reading frame (DWORF) polypeptide, operably linked to a promoter, the expression cassette flanked by inverted terminal repeats. The disclosure further provides pharmaceutical compositions and methods of treating or preventing heart disease.

[Continued on next page]

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