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(54) Title: NON-VIRAL DNA VECTORS AND USES THEREOF FOR EXPRESSING PHENYLALANINE HYDROXYLASE (PAH) THERAPEUTICS

(57) Abstract: The application describes ceDNA vectors having linear and continuous structure for delivery and expression of a transgene. ceDNA vectors comprise an expression cassette flanked by two ITR sequences, where the expression cassette encodes a transgene encoding PAH protein. Some ceDNA vectors further comprise cis-regulatory elements, including regulatory switches. Further provided herein are methods and cell lines for reliable gene expression of PAH protein *in vitro, ex vivo* and *in vivo* using the ceDNA vectors. Provided herein are method and compositions comprising ceDNA vectors useful for the expression of PAH protein in a cell, tissue or subject, and methods of treatment of diseases with said ceDNA vectors expressing PAH protein. Such PAH protein can be expressed for treating disease, *e.g.*, Phenylketonuria (PKU).