CLAIMS

1. A combination of (i) a viral vector comprising a transgene encoding for a protein of interest, and (ii) an extracellular vesicle (EV)-based vector comprising the transgene in the form of mRNA, circular RNA (circRNA), mini-circle, and/or plasmid DNA (pDNA) for use in combination therapy, in which the transgene is to be initially administered using the viral vector and to be subsequently administered using the EV-based vector.

2. A combination of (i) a viral vector comprising a transgene encoding for a protein of interest, and (ii) an extracellular vesicle (EV)-based vector comprising the transgene in the form of mRNA, circular RNA (circRNA), mini-circle, and/or plasmid DNA (pDNA) for use in combination therapy in the treatment of a genetic disease, in which the transgene is to be initially administered using the viral vector and to be subsequently administered using the EV-based vector.

3. A combination therapy for use, according to Claim 2, in which the genetic disease is selected from the group consisting of lysosomal storage disorders, inherited errors of metabolism, myopathies, peroxisomal disorders, mitochondrial diseases, neurological and neurodegenerative diseases, inflammatory diseases and cancer.

4. A combination therapy for use, according to Claim 1, 2 or 3, in which the transgene is to be administered in a first dose using the viral vector and in second (and optionally subsequent) dose(s) using the EV-based vector.

5. A combination therapy for use, according to any preceding claim, in which the transgene encodes for a peptide and/or a polypeptide.

6. A combination therapy for use, according to any preceding claim, in which the viral vector is a retrovirus, vesicular stomatitis virus, an adenovirus, an adeno-associated virus, a lentivirus, a herpes simplex virus, a coxsackie virus, or any other type of virus.

7. A combination therapy for use, according to any preceding claim, in which the EV-based vector is an exosome and/or a microvesicle.

8. A combination therapy for use, according to any preceding claim, in which the EV-based vector is exogenously or endogenously modified to contain the transgene.

9. A combination therapy for use, according to Claim 8, in which the EV-based vector is modified to comprise a fusion protein comprising an EV protein and a nucleic acid (NA)-binding protein, in which the NA-binding protein interacts with and loads the mRNA, circRNA, mini-circle and/or pDNA transgene into the EV-based vector.

10. A method of manufacturing a combination therapy for use, according to any preceding claim, comprising the steps of:

(a) infecting a first host cell with a viral vector genome comprising the transgene and collecting the viral vectors produced by the first host cell; and,

(b) genetically modifying a second host cell to produce EV-based vectors comprising the transgene in an mRNA, circRNA, mini-circle and/or pDNA polynucleotide and collecting the EV-based vectors produced by the second host cell,

in which steps (a) and (b) may be carried out sequentially in any order or in parallel.

11. A method according to Claim 10, in which the first host cell and the second host cell are of the same cell type.

12. A method according to Claim 10 or 11, in which the genetic modification in step (b) comprises expressing in the second host cell a fusion protein comprising an EV protein and a NA-binding protein, in which the NA-binding protein interacts with and loads the mRNA, circRNA, mini-circle DNA and/or pDNA transgene into the EV-based vector.

13. A method according to Claim 10, 11 or 12, further comprising the step of formulating the viral vector and the EV-based vector in one or more separate pharmaceutical compositions.

14. Use of a combination comprising (i) a viral vector comprising a transgene encoding for a protein of interest, and (ii) an extracellular vesicle (EV)-based vector comprising the transgene in the form of mRNA, circular RNA (circRNA), mini-circle, and/or plasmid DNA (pDNA) in the preparation of a medicament for the treatment of a genetic disease in a subject, in which the transgene is to be initially administered using the viral vector and to be subsequently administered using the EV-based vector.