Claims

1. A combination therapy, comprising (i) a viral vector comprising a transgene encoding for a protein of interest, and (ii) an EV-based vector comprising the transgene in the form of mRNA, circular RNA (circRNA), mini-circle, and/or plasmid DNA (pDNA).
2. The combination therapy according to claim 1, wherein the transgene is initially administered using the viral vector and subsequently administered using the EV-based vector.
3. The combination therapy according to any one of the preceding claims, wherein the transgene is administered in a first dose using the viral vector and in second (and optionally subsequent) dose(s) using the EV-based vector.
4. The combination therapy according to any one of the preceding claims, wherein the transgene encodes for a peptide and/or a polypeptide.
5. The combination therapy according to any one of the preceding claims, wherein 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 native or recombinant virus.
6. The combination therapy according to any one of the preceding claims, wherein the EV-based vector is an extracellular vesicle, an exosome, and/or a microvesicle.
7. The combination therapy according to any one of the preceding claims, wherein the EV-based vector is exogenously or endogenously modified to contain the transgene.
8. The combination therapy according to claim 7, wherein the EV-based vector is modified to comprise a fusion protein comprising an EV protein and a nucleic acid (NA)-binding protein, wherein said NA-binding protein interacts with and loads the mRNA, circRNA, mini-circle and/or pDNA transgene into the EV-based vector.
9. The combination therapy according to any one of the preceding claims, for use in medicine.
10. The combination therapy according to any one of the preceding claims, for use in the treatment of genetic diseases.

11. The combination therapy according to claim 10, wherein the genetic diseases are selected from the group comprising lysosomal storage disorders, inherited errors of metabolism, myopathies, peroxisomal disorders, mitochondrial diseases, neurological and neurodegenerative diseases, inflammatory diseases and cancer.
12. A method of manufacturing a combination therapy according to any one of claims 1-11, 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 said first host cell; and,
    (b) genetically modifying a second host cell to produce EV-based vectors comprising said transgene in an mRNA, circRNA, mini-circle and/or pDNA polynucleotide and collecting the EV-based vectors produced by the second host cell,

    wherein steps (a) and (b) may be carried out sequentially in any order or in parallel.
13. The method according to claim 12, wherein the first host cell and the second host cell are the of the same cell type.
14. The method according to any one of claims 12-13, wherein 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, wherein said NA-binding protein interacts with and loads the mRNA, circRNA, mini-circle DNA and/or pDNA transgene into the EV-based vector.
15. The method according to any one of claims 12-14, further comprising the step of formulating the viral vector and the EV-based vector in one or more pharmaceutical composition.