Claims

1. **A combination** comprising or consisting of
(i) at least one first component comprising at least one therapeutic RNA; and
(ii) at least one second component comprising at least one antagonist of at least one RNA sensing pattern recognition receptor,
wherein the at least one therapeutic RNA of the first component is selected from a coding RNA.

2. Combination of **claim 1**, wherein the at least one RNA sensing pattern recognition receptor induces cytokines upon binding of an RNA agonist and/or.

~~**3.** Combination of **claim 1 or 2**, wherein the at least one RNA sensing pattern recognition receptor inhibits translation upon binding of an RNA agonist.~~

43. Combination of **any of the preceding claims**, wherein the at least one antagonist of the second component reduces cytokine induction by the at least one RNA sensing pattern recognition receptor upon binding of an RNA agonist and/or reduces translation inhibition by the at least one RNA sensing pattern recognition receptor upon binding of an RNA agonist and/or.

~~**5.** Combination of **any of the preceding claims**, wherein administration of the combination of the at least one therapeutic RNA of the first component and the at least one antagonist of at least one RNA sensing pattern recognition receptor of the second component to be administered leads to a reduced innate immune response compared to administration of the at least one therapeutic RNA of the first component without combination with the at least one antagonist of at least one RNA sensing pattern recognition receptor of the second component to be administered.~~

~~**6.** Combination of **claim 5**, wherein the induction of an innate immune response is determined by measuring the induction of cytokines.~~

~~**7.** Combination of **claim 6**, wherein the cytokines are selected from the group consisting of IFN-α, TNF-α, IP-10, IFN-γ, IL-6, IL-12, IL-8, Rantes, MIP-1 alpha, MIP-1 beta, McP1, or IFNbeta.~~

~~**8.** Combination of **claim 6 or 7**, wherein the induction of cytokines is measured by administration of the combination into cells, a tissue or an organism, preferably hPBMCs, Hela cells or HEK cells.~~

~~**9.** Combination of **any of the preceding claims**, wherein the at least one RNA sensing pattern recognition receptor is an endosomal receptor or a cytoplasmic receptor, *preferably* an endosomal receptor.~~

~~10~~**4.** Combination of **any of the preceding claims**, wherein the at least one RNA sensing pattern recognition receptor is a receptor for single stranded RNA (ssRNA) and/or a receptor for double stranded RNA (dsRNA).

~~11~~5. Combination of **any of the preceding claims**, wherein the at least one RNA sensing pattern recognition receptor is selected from a Toll-like receptor (TLR), a Retinoic acid-inducible gene-I-like receptor (RLR), a NOD-like receptor, PKR, OAS, SAMHD1, ADAR1, IFIT1 and/or IFIT5~~.~~, preferably

~~**12.** Combination of **claim 11,** wherein the at least one Toll-like receptor is selected from TLR3, TLR7, TLR8 and/or TLR9.~~, more preferably

~~**13.** Combination of **claim 11 or 12**, wherein the at least one Toll-like receptor is selected from TLR8 and/or TLR9, most preferably from a TLR7 and /or TLR8~~, and, optionally, ~~.~~

~~**14.** Combination of **claim 11,** wherein the Retinoic acid-inducible gene-I-like receptor (RLR) is selected from RIG-1, MDA5, LGP2, cGAS, AIM2, NLRP3, NOD2, preferably RIG1 and/or MDA5.~~

~~**15.** Combination of **any one of the preceding claims**, wherein the at least one antagonist of the second component is selected from a nucleotide, a nucleotide analog, a nucleic acid, a peptide, a protein, a small molecule, a lipid, or a fragment, variant or derivative of any of these.~~

~~16~~6. Combination of **any one of the preceding claims**, wherein the at least one antagonist of the second component is a nucleic acid~~, preferably.~~

~~**17.** Combination of **any one of the preceding claims**, wherein the at least one antagonist of the second component is~~ a single stranded nucleic acid~~, and/or .~~

~~**18**.~~ Combination of **~~claim 16 or 17~~**, wherein the nucleic acid of the second component comprises or consists of nucleotides selected from DNA nucleotides, RNA nucleotides, PNA nucleotides, and/or LNA nucleotides, or analogs or derivatives of any of these.

~~19~~7. Combination of **~~any one of claims 16 to 18~~6**, wherein the nucleic acid of the second component comprises at least one modified nucleotide and/or at least one nucleotide analogue or nucleotide derivative~~.~~.

~~**20.** Combination of **claim 19,** wherein the at least one modified nucleotide and/or at least one nucleotide analogues is~~ preferably selected from a backbone modified nucleotide, a sugar modified nucleotide and/or a base modified nucleotide, or any combination thereof~~, more preferably.~~

~~**21.** Combination of any one of **claims 19 or 20**~~, wherein the least one modified nucleotide and/or the at least one nucleotide analog is selected from 1-methyladenosine, 2-methyladenosine, N6-methyladenosine, 2'-O-methyladenosine, 2-methylthio-N6-methyladenosine, N6-isopentenyladenosine, 2-methylthio-N6-isopentenyladenosine, N6-threonylcarbamoyladenosine, 2-methylthio-N6-threonyl carbamoyladenosine, N6-methyl-N6-threonylcarbamoyladenosine, N6-hydroxynorvalylcarbamoyladenosine, 2-methylthio-N6-hydroxynorvalyl carbamoyladenosine, inosine, 3-methylcytidine , 2'-O-methylcytidine, 2-thiocytidine, N4-acetylcytidine, lysidine, 1-methylguanosine, 7-methylguanosine, 2'-O-methylguanosine, queuosine, epoxyqueuosine, 7-cyano-7-deazaguanosine, 7-aminomethyl-7-deazaguanosine, pseudouridine, dihydrouridine, 5-methyluridine, 2'-O-methyluridine,

2-thiouridine, 4-thiouridine, 5-methyl-2-thiouridine, 3-(3-amino-3-carboxypropyl)uridine´, 5-hydroxyuridine, 5-methoxyuridine, uridine 5-oxyacetic acid, uridine 5-oxyacetic acid methyl ester, 5-aminomethyl-2-thiouridine, 5-methylaminomethyluridine, 5-methylaminomethyl-2-thiouridine, 5-methylaminomethyl-2-selenouridine, 5-carboxymethylaminomethyluridine, 5-carboxymethylaminomethyl- 2'-O-methyluridine, 5-carboxymethylaminomethyl-2-thiouridine, 5-(isopentenylaminomethyl)uridine, 5-(isopentenylaminomethyl)- 2-thiouridine, or 5-(isopentenylaminomethyl)- 2'-O-methyluridine.

~~**22.** Combination of any one of **claims 19 to 21,**~~ 8. Combination of claim 7, wherein the at least one modified nucleotide is a sugar modified nucleotide, preferably a 2' ribose modified RNA nucleotide, more preferably.

~~**23.** Combination of **claim 22**, wherein the 2' ribose modified RNA nucleotide is~~ a 2'-O-methylated RNA nucleotide.

~~**24.** Combination of **claim 23**,~~ wherein the 2'-O-methylated RNA nucleotide is more preferably selected from

2'-O-methylated guanosine (Gm), a 2'-O-methylated uracil (Um), a 2'-O-methylated adenosine (Am), a 2'-O-methylated cytosine (Cm), or a 2'-O-methylated analogue of any of these nucleotides.

9~~25~~. Combination of **any one of claims ~~16~~ 6 to ~~24~~8**, wherein the nucleic acid of the second component comprises at least one or more trinucleotide M-X-Y motifs,
wherein M is selected from Gm, Um, or Am, preferably wherein M is Gm;
wherein X is selected from G, A, or U, *preferably* wherein X is G; and
wherein Y is selected from G, A, U, C, or dihydrouridine, *preferably* wherein Y is C, and/or.

~~**26.** Combination of **any one of claims 16 to 25**,~~ wherein the nucleic acid of the second component comprises or consists of a nucleic acid sequence according to formula I:

$$N_W\text{-}M\text{-}X\text{-}Y\text{-}N_Z \qquad \text{(Formula I)}$$

wherein N is independently selected from G, A, U, C, Gm, Am, Um, Cm, or a modified nucleotide;
wherein W is 0 or an integer of 1 to 15;
wherein Z is 0 or an integer of 1 to 15;
wherein M, X, and Y are selected as defined ~~in claim 25~~before, optionally.

~~**27.** Combination of **any one of claims 16 to 26**,~~ wherein the nucleic acid of the second component comprises or consists of at least 2, 3, 4, 5, 6, 7, 8, 9, 10 or more nucleic acid sequences according to formula I, wherein each of the at least 2, 3, 4, 5, 6, 7, 8, 9, 10 or more nucleic acid sequences according to formula I are identical or independently selected from each other, and/or.

~~**28.** Combination of **any one of claims 16 to 27**, wherein~~ the nucleic acid of the second component contains a 5′ end that is devoid of a triphosphate group.

~~29.~~ Combination of ~~any one of claims 16 to 27~~, wherein the nucleic acid of the second component contains a triphosphate group at the 5' end.

~~30~~10. Combination of **any one of claims ~~16~~ 6 to ~~29~~9**, wherein the nucleic acid of the second component has a length of about 3 to about 50 nucleotides, about 5 to about 25 nucleotides, about 5 to about 15, or about 5 to about 10 nucleotides, *preferably* about 5 to about 15 nucleotides, optionally~~.~~

~~31.~~ Combination of ~~any one of claims 16 to 30~~, wherein the nucleic acid of the second component has a length of 5 nucleotides, 6 nucleotides, 7 nucleotides, 8 nucleotides, 9 nucleotides, 10 nucleotides, 11 nucleotides, 12 nucleotides, or 13 nucleotides, *preferably* 9 nucleotides.

~~32~~11. Combination of **any one of claims ~~16~~ to ~~31~~10**, wherein the nucleic acid of the second component is a single stranded oligonucleotide, preferably~~.~~

~~33.~~ Combination of ~~claim 32~~, wherein the single stranded oligonucleotide is a single stranded RNA oligonucleotide.

~~34~~12. Combination of **any one of claims ~~16~~ 6 to ~~33~~11**, wherein the nucleic acid of the second component, comprises or consists of a nucleic acid sequence derived from a bacterial tRNA, preferably a bacterial $tRNA^{Tyr}$, optionally~~.~~

~~35.~~ Combination of ~~claim 34~~, wherein the nucleic acid sequence is or is derived from a bacterial $tRNA^{Tyr}$, preferably from the D-Loop of a bacterial $tRNA^{Tyr}$, most *preferably* the D-Loop of Escherichia coli $tRNA^{Tyr}$.

~~36~~13. Combination of **any one of claims ~~16~~ to ~~35~~12**, wherein the nucleic acid of the second component comprises or consists of a nucleic acid sequence identical or at least 70%, 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a nucleic acid sequence selected from the group consisting of **SEQ ID NOs: 85-212**, or fragments of any of these sequences, preferably~~.~~

~~37.~~ Combination of ~~claim 36~~, wherein the nucleic acid of the second component comprises or consists of a nucleic acid sequence identical or at least 70%, 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a nucleic acid sequence selected from the group consisting of **SEQ ID NOs: 85-87, 149-212**, or fragments of any of these sequences, more *preferably* wherein the nucleic acid of the second component comprises or consists of a nucleic acid sequence identical or at least 70%, 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a nucleic acid sequence according to 5'-GAG CGmG CCA-3' (**SEQ ID NO: 85**), or a fragment thereof.

~~38.~~ Combination of ~~any one of the preceding claims~~, wherein the at least one therapeutic RNA of the first component is selected from a coding RNA, a non-coding RNA, a circular RNA (circRNA), an RNA oligonucleotide, a small interfering RNA (siRNA), a small hairpin RNA (shRNA), an antisense RNA (asRNA), a CRISPR/Cas9 guide RNAs, an mRNA, a riboswitch, a ribozyme, an RNA aptamer, a

~~ribosomal RNA (rRNA), a transfer RNA (tRNA), a viral RNA (vRNA), a retroviral RNA, a small nuclear RNA (snRNA), a self-replicating RNA, a replicon RNA, a small nucleolar RNA (snoRNA), a microRNA (miRNA), and a Piwi-interacting RNA (piRNA).~~

~~39~~14. Combination of **any of the preceding claims**, wherein the at least one therapeutic RNA of the first component is an in vitro transcribed RNA, preferably.

~~40.~~ Combination of ~~**claim 39**~~, wherein the in vitro transcribed RNA is obtainable by RNA in vitro transcription using a sequence optimized nucleotide mixture, and/or.

~~41.~~ Combination of ~~**any of the preceding claims**~~, wherein at least one therapeutic RNA of the first component is a purified RNA.

~~42.~~ Combination of ~~**claim 41**~~, wherein the purified RNA is more *preferably* purified by RP-HPLC and/or TFF and/or Oligo d(T) purification.

~~43.~~ Combination of ~~**any one of the preceding claims**~~, ~~wherein the at least one therapeutic RNA of the first component is a coding RNA.~~

~~44~~15. Combination of ~~**claim 43**~~,**any of the preceding claims,** wherein the coding RNA is selected from an mRNA, a self-replicating RNA, a circular RNA, a viral RNA, or a replicon RNA, preferably from an mRNA.

~~45.~~ Combination of ~~**any one of the preceding claims**~~, ~~wherein the at least one therapeutic RNA of the first component is an mRNA.~~

~~46.~~ Combination of ~~**any one of claims 43 to 45**~~, wherein the coding RNA or the mRNA comprises at least one coding sequence encoding at least one peptide or protein, preferably.

~~47.~~ Combination of ~~**claim 46**~~, wherein the expression of the encoded at least one peptide or protein of the coding RNA or the mRNA is increased or prolonged by the combination with the at least one antagonist of at least one RNA sensing receptor of the second component ~~upon administration~~ to be administered into cells, a tissue or an organism compared to the expression of the encoded at least one peptide or protein of the coding RNA or the mRNA without combination with the at least one antagonist of at least one RNA sensing pattern recognition receptor of the second component.

~~48.~~ Combination of ~~**claim 46 to 47**~~, wherein the at least one peptide or protein is or is derived from a therapeutic peptide or protein.

~~49.~~ Combination of ~~**claim 48**~~, wherein the therapeutic peptide or protein preferably is or is preferably derived from an antibody, an intrabody, a receptor, a receptor agonist, a receptor antagonist, a binding protein, a CRISPR-associated endonuclease, a chaperone, a transporter protein, an ion channel, a membrane protein, a secreted protein, a transcription factor, an enzyme, a peptide or protein hormone,

a growth factor, a structural protein, a cytoplasmic protein, a cytoskeletal protein, a viral antigen, a bacterial antigen, a protozoan antigen, an allergen, a tumor antigen, or fragments, variants, or combinations of any of these~~.~~.

~~**50.** Combination of **any one of claims 46 to 49**,~~ wherein the at least one coding sequence is more *preferably* a codon modified coding sequence, ~~wherein the amino acid sequence encoded by the at least one codon modified coding sequence is preferably not being modified compared to the amino acid sequence encoded by the corresponding wild type coding sequence.~~

~~**51.** Combination of **claim 50**,~~ wherein the at least one codon modified coding sequence is most *preferably* selected from C maximized coding sequence, CAI maximized coding sequence, human codon usage adapted coding sequence, G/C content modified coding sequence, and G/C optimized coding sequence, or any combination thereof.

~~52~~**16.** Combination of **any one of the preceding claims**, wherein the at least one therapeutic RNA of the first component, *preferably* the mRNA, comprises a 5'-cap structure, preferably~~.~~

~~**53.** Combination of **claim 52**,~~ wherein the 5'-cap structure is a cap0, cap1, cap2, a modified cap0 or a modified cap1 structure, more preferably~~.~~

~~**54.** Combination of **claim 53**, wherein~~ the 5'-cap structure is a cap1 structure.

~~**55.** Combination of **claim 54**, wherein the cap1 structure is obtainable by co-transcriptional capping using a trinucleotide cap1 analog.~~

~~**56.** Combination **any one of the preceding claims**, wherein about 70%, 75%, 80%, 85%, 90%, 95% of the therapeutic RNA (species) of the first component comprises a cap1 structure as determined using a capping detection assay.~~

~~57~~**17.** Combination of **any one of the preceding claims**, wherein the at least one therapeutic RNA of the first component comprises at least one modified nucleotide or a modified nucleotide analogue~~.~~.

~~**58.** Combination of **claim 57**,~~ wherein the at least one modified nucleotide is preferably selected from pseudouridine (ψ), N1-methylpseudouridine (m1ψ), 5-methylcytosine, and/or 5-methoxyuridine.

~~59~~**18.** Combination of **any one of the preceding claims**, wherein the at least one therapeutic RNA of the first component, *preferably* the mRNA, comprises at least one poly(A) sequence, and/or at least one poly(C) sequence, and/or at least one histone stem-loop sequence/structure~~.~~, preferably

~~**60.** Combination of **claim 59**,~~ wherein the poly(A) sequence is located at the 3' terminus of the therapeutic RNA, and/or wherein the 3' terminus of the RNA consists of a poly(A) sequence terminating with an A nucleotide and/or~~.~~

~~**61.** Combination of **any one of the preceding claims**,~~ wherein the at least one therapeutic RNA of the first component, *preferably* the mRNA, comprises at least one heterologous 5'-UTR and/or at least one heterologous 3'-UTR~~.~~

~~**62.** Combination of **claim 61**,~~ wherein the at least one heterologous 3'-UTR comprises a nucleic acid sequence preferably derived from a 3'-UTR of a gene selected from PSMB3, ALB7, alpha-globin, CASP1, COX6B1, GNAS, NDUFA1 and RPS9, or from a homolog, a fragment or a variant of any one of these genes or~~.~~

~~**63.** Combination of **claim 61**,~~ wherein the at least one heterologous 5'-UTR comprises a nucleic acid sequence preferably derived from a 5'-UTR of a gene selected from HSD17B4, RPL32, ASAH1, ATP5A1, MP68, NDUFA4, NOSIP, RPL31, SLC7A3, TUBB4B and UBQLN2, or from a homolog, a fragment or variant of any one of these genes.

~~64~~**19.** Combination of **any one of the preceding claims**, wherein the at least one antagonist of the second component, *preferably* the nucleic acid, and/or the at least one therapeutic RNA of the first component is complexed or associated with or at least partially complexed or partially associated with one or more cationic or polycationic compound, *preferably* cationic or polycationic polymer, cationic or polycationic polysaccharide, cationic or polycationic lipid, cationic or polycationic protein, or cationic or polycationic peptide, or any combinations thereof, preferably~~.~~

~~**65.** Combination of **claim 64**, wherein the one or more cationic or polycationic peptides are selected from **SEQ ID NO: 39 to 43**, or any combinations thereof.~~

~~**66.** Combination of **claim 64**, wherein the cationic or polycationic polymer is a polyethylene glycol/peptide polymer comprising HO-PEG5000-S-(S-CHHHHHHHRRRRRHHHHHHC-S-)7-S-PEG5000-OH (**SEQ ID NO: 42** of the peptide monomer) and/or a polyethylene glycol/peptide polymer comprising HO-PEG5000-S-(S-CGHHHHHRRRRRHHHHHGC-S-)4-S-PEG5000-OH (**SEQ ID NO: 43** of the peptide monomer).~~

~~**67.** Combination of **claim 65 or 66**, additionally comprising a lipid and/or a lipidoid.~~

~~**68.** Combination of **any of the proceeding claims**,~~ wherein the at least one antagonist of the second component, *preferably* the nucleic acid, and/or the at least one therapeutic RNA of the first component is complexed, partially complexed, encapsulated, partially encapsulated, or associated with one or more lipids, thereby forming liposomes, lipid nanoparticles (LNP), lipoplexes, and/or nanoliposomes, *preferably* lipid nanoparticles (LNP)~~.~~

~~**69.** Combination of **claim 68**,~~ wherein the LNP more preferably comprises
(i) at least one cationic lipid, *preferably* lipid III-3;
(ii) at least one neutral lipid, *preferably* 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC);
(iii) at least one steroid or steroid analogue, *preferably* cholesterol; and
(iv) at least one PEG-lipid, *preferably* a PEGylated lipid of formula (IVa),

preferably wherein (i) to (iv) are in a molar ratio of about 20-60% cationic lipid; 5-25% neutral lipid; 25-55% sterol; 0.5-15% PEG-lipid.

~~70~~**20.** **Pharmaceutical composition** comprising or consisting of a combination as defined in **any one of claims 1 to ~~69~~19**, and *optionally* at least one pharmaceutically acceptable carrier~~.~~, preferably

~~**71.** Pharmaceutical composition of **claim 70** wherein the at least one therapeutic RNA and the at least one antagonist are formulated separately.~~

~~**72.** Pharmaceutical composition of **claim 71** wherein the at least one therapeutic RNA and the at least one antagonist are~~ more preferably co-formulated to increase the probability that they are both present in one particle to ensure that the at least one therapeutic RNA and the at least one antagonist are uptaken by the same cell.

~~73~~**21.** Pharmaceutical composition of ~~**any one of claims 70 to 72**~~**claim 20**, wherein the molar ratio of the at least one antagonist, *preferably* the nucleic acid, to the at least one therapeutic RNA ranges from about 1:1, to about 100:1, or ranges from about 20:1, to about 80:1 and/or~~.~~

~~**74.** Pharmaceutical composition of **any one of claims 70 to 73**, wherein the weight to weight ratio of the at least one antagonist, *preferably* the nucleic acid, to the at least one therapeutic RNA ranges from about 1:1, to about 1:30, or ranges from about 1:2, to about 1:10.~~

~~75~~**22.** Pharmaceutical composition of **any one of claims ~~70 to 74~~20 and 21**, wherein ~~administration of~~ the composition is to be administered to a cell, tissue, or organism results in essentially the same or at least a comparable activity of the therapeutic RNA as compared to ~~administration of~~ a corresponding therapeutic RNA to be administered only, or~~.~~

~~**76.** Pharmaceutical composition of **any one of claims 70 to 74**, wherein administration of the composition is to be administered to a cell, tissue, or organism results in increased activity of the therapeutic RNA *for example* as compared to ~~administration of~~ a corresponding therapeutic RNA to be administered only~~**

~~**77.** Pharmaceutical composition of **claims 75 or 76**, wherein activity of the therapeutic RNA is preferably expression of an encoded peptide or protein, more *preferably* protein expression.~~

~~78~~**23.** Pharmaceutical composition of **any one of claims ~~70 to 77~~20 to 22**, wherein ~~administration of~~ the composition is to be administered to a cell, tissue, or organism results in a reduced (innate) immune stimulation as compared to ~~administration of~~ the corresponding therapeutic RNA to be administered only.

~~79~~**24.** Kit or kit of parts comprising at least one first and at least one second component as defined in **any one of claims 1 to ~~69~~19**, and/or at least one pharmaceutical composition as defined in **any one of claims ~~70 to 78~~20 to 23**, *optionally* comprising a liquid vehicle for solubilising, and, *optionally*, technical instructions providing information on administration and/or dosage of the components.

~~80~~25. Combination of **any one of claims 1 to ~~69~~19**, pharmaceutical composition of **any one of claims ~~70 to 78~~20 to 23**, or kit or kit of parts of **claim ~~79~~ 24** for use as a medicament.

~~81~~26. Combination of **any one of claims 1 to ~~69~~19**, pharmaceutical composition of **any one of claims ~~70 to 78~~20 to 23**, or kit or kit of parts of **claim ~~79~~ 24** for use in a chronic medical treatment, or ~~.~~

~~**82.** Medical use of **claim 81**, wherein in the chronic medical treatment administration of the combination, the composition, the kit or kit of parts, is performed more than once, for example once or more than once a day, once or more than once a week, once or more than once a month.~~

~~**83.** Combination of **any one of claims 1 to 69**, pharmaceutical composition of **any one of claims 70 to 78**, or kit or kit of parts of **claim 79** for use in the treatment or prophylaxis of an infection, *preferably* a virus infection, a bacterial infection, or a protozoan infection, or~~.

~~**84.** Combination of **any one of claims 1 to 69**, pharmaceutical composition of **any one of claims 70 to 78**, or kit or kit of parts of **claim 79** for~~ use in the treatment or prophylaxis of a tumour disease, or of a disorder related to such tumour disease or~~.~~

~~**85.** Combination of **any one of claims 1 to 69**, pharmaceutical composition of **any one of claims 70 to 78**, or kit or kit of parts of **claim 79** for use in the treatment or prophylaxis of a genetic disorder or condition or~~.~~

~~**86.** Combination of **any one of claims 1 to 69**, pharmaceutical composition of **any one of claims 70 to 78**, or kit or kit of parts of **claim 79** for use in the treatment or prophylaxis of a protein or enzyme deficiency.~~

~~**87.** A method of treating or preventing a disorder, disease, or condition, wherein the method comprises applying or administering to a subject in need thereof the combination as defined in **any one of claims 1 to 69**, the pharmaceutical composition as defined in **any one of claims 70 to 78**, or the kit or kit of parts as defined in **claim 79**.~~

~~**88.** Method of **claim 87**, wherein administration of the first component and the second component is essentially simultaneous.~~

~~**89.** Method of **claim 87**, wherein administration of the first component and the second component is sequential.~~

~~**90.** Method of **any one of claims 86 to 89**, wherein administration of the combination, the pharmaceutical composition, the kit or kit of parts, is performed more than once, for example once or more than once a day, once or more than once a week, once or more than once a month.~~

~~**91.** A method of **any one of claims 86 to 90**, wherein the administration or applying is subcutaneous, intravenous, intramuscular, intra-articular, intra-synovial, intranasal, oral, intrasternal, intrathecal,~~

~~intrahepatic, intralesional, intracranial, transdermal, intradermal, intrapulmonal, intraperitoneal, intracardial, intraarterial, intraocular, intravitreal, subretinal, or intratumoral.~~

~~**92.** Method of **any one of claims 86 to 91**, wherein the subject in need is a mammalian subject, preferably a human subject.~~

~~**93.** Method of reducing the (innate) immune stimulation of a therapeutic RNA wherein the method comprises applying or administering to a subject in need thereof the combination as defined in **any one of claims 1 to 69**, the pharmaceutical composition as defined in **any one of claims 70 to 78**, or the kit or kit of parts as defined in **claim 79**.~~

~~**94.** Method of increasing and/or prolonging the expression of a peptide or protein encoded by a (coding) therapeutic RNA wherein the method comprises applying or administering to a subject in need thereof the combination as defined in **any one of claims 1 to 69**, the pharmaceutical composition as defined in **any one of claims 70 to 78**, or the kit or kit of parts as defined in **claim 79**.~~