Interestingly, IFNλ retains many antiviral properties despite the less inflammatory response compared with type I IFNs. This has spurred development of IFNλ for clinical use as an alternative treatment to IFNα for HCV infection (Muir et al., J. Hepatol. 61 (2014), 1238-1246). More recent developments also indicate that IFNλ treatment could also be utilized to control respiratory viral infections. IFNλ2 and 3 was shown to control IAV pulmonary titers similarly to IFNα or IFNβ treatment (Davidson et al., EMBO Mol. Med. 8 (2016), 1099-1112; Kim et al, Am. J. Respir. Cell. Mol. Biol. 56 (2017), 202-212). Importantly, IFNλ treatment avoided excessive pulmonary inflammation associated with IFNα treatment (Kim et al., Am. J. Respir. Cell. Mol. Biol. 56 (2017), 202-212). Therapeutic applications of IFNλ so far concentrate on the administration of the recombinantly produced protein. However, the use of recombinantly produced protein requires the repeated administration of relatively high doses of protein since the protein is relatively quickly cleared from the system and can, thus, only act for a brief period of time. For example in Dinnon III et al. (Nature https://doi.org/10.1038/s41586-020-2708-8 (2020)) 2 μg of peg-IFNλ1 is administered subcutaneously to mice. Similarly, Davidson et al. (EMBO Mol. Med. 8 (2016), 1099-1112) describe the administration of 2.6 μg/50μl of IFNλ3 to B6.A2G-Mx mice for treating or preventing influenza infection. In Galani et al. (Immunity 46 (2017), 875-890), it was reported that mice were treated with 5 or 10 μg of recombinant mouse pegylated IFNλ2.

Therefore, there is a need to provide means and methods for an efficient way to deliver IFNλ *in vivo* to target tissues, i.e. in a manner which ensures that it is active for an extended period of time and can exert its effect for an extended period of time. This would allow to reduce the amount of IFNλ to be administered to a patient within a given period of time and would also allow to reduce the numbers of administrations to a patient.

The present invention addresses this need by providing the embodiments as recited in the claims.

Summary
In one aspect, the present disclosure provides a use of a pharmaceutical composition comprising an mRNA encoding an IFN-λ1 polypeptide in the manufacture of a medicament for treating or preventing a viral-induced disorder, wherein the medicament is to be administered by delivery into the respiratory system, wherein said viral-induced disorder is a viral-induced respiratory disorder.

Thus, the present invention relates to a pharmaceutical composition comprising an mRNA encoding an IFN-λ polypeptide for use in treating and/or preventing a viral-induced disorder.

CLAIMS

1. Use of a pharmaceutical composition comprising an mRNA encoding an IFN-λ1 polypeptide in the manufacture of a medicament for treating or preventing a viral-induced disorder, wherein the medicament is to be administered by delivery into the respiratory system, wherein said viral-induced disorder is a viral-induced respiratory disorder.

2. The use of claim 1, wherein the virus which causes said viral-induced respiratory disorder is selected from the group consisting of rhinovirus, influenza virus, parainfluenza virus, metapneumo virus, respiratory syncytial virus, adenovirus and corona virus.

3. The use of claims 1 or 2, wherein the virus which causes said viral-induced respiratory disorder is a virus which enters cells via the ACE2 receptor.

4. The use of claim 3, wherein said virus is SARS- CoV, SARS-CoV-2 or HCoV-NL63.

5. The use of any one of claims 1 to 4, wherein said delivery into the respiratory system is by instillation or inhalation.

6. The use of claim 5, wherein said inhalation is inhalation of an aerosol comprising said mRNA.

7. The use of any one of claims 1 to 6, wherein the mRNA contains a combination of unmodified and modified nucleotides.

8. The use of claim 7, wherein the total percentage of modified nucleotides comprised in the mRNA molecules is 2.5% to 100%; more preferably wherein 5 to 50% of the uridine nucleotides and 5 to 50% of the cytidine nucleotides are modified uridine nucleotides and modified cytidine nucleotides, respectively, and wherein preferably the modified uridine nucleotides are 2-thiouridine and the modified cytidine nucleotides are 5-methylcytidine.

9. The use of claim 7 or 8, wherein the modified nucleotides are selected from the following list based on their respective nucleoside residue: pseudo-uridine, N1-

methyl-pseudo-uridine, 2´-fluoro-2´-deoxycytidine, 5-iodocytidine, 5-methylcytidine, 2-thiouridine, 5-iodouridine and/or 5-methyl-uridine.

10. The use of any one of claims 1 to 9, wherein the coding region of the mRNA coding for IFN-λ1 is a partly or fully codon optimized sequence.

11. The use of any one of claims 1 to 10, wherein the coding region of the mRNA coding for IFNλ1 is as shown in SEQ ID NO: 1.

12. The use of any one of claims 1 to 11, wherein the mRNA coding for IFNλ1 has a sequence as shown in SEQ ID NO: 13.

13. The use of any one of claims 1 to 12 further comprising an mRNA encoding a type I interferon and/or an mRNA encoding a type II interferon.

14. The use of claim 13, wherein the type I interferon is selected from the group consisting of IFN-α, preferably IFN-α16, and IFN-β, and wherein the type II interferon is IFNγ.