

CLAIMS

What is claimed is:

1. A pharmaceutical composition comprising:
 - (a) a herpes virus comprising a recombinant herpes virus genome, wherein the recombinant herpes virus genome comprises one or more polynucleotides encoding a cystic fibrosis transmembrane conductance regulator (CFTR) polypeptide; and
 - (b) a pharmaceutically acceptable excipient,wherein the pharmaceutical composition is suitable for nebulization.
2. The pharmaceutical composition of claim 1, wherein the recombinant herpes virus genome is replication defective.
3. The pharmaceutical composition of claim 1 or claim 2, wherein the CFTR polypeptide comprises a sequence having at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO: 5 or SEQ ID NO: 6.
4. The pharmaceutical composition of any one of claims 1-3, wherein the recombinant herpes virus genome is a recombinant herpes simplex virus genome.
5. The pharmaceutical composition of claim 4, wherein the recombinant herpes simplex virus genome is a recombinant type 1 herpes simplex virus (HSV-1) genome, a recombinant type 2 herpes simplex virus (HSV-2) genome, or any derivatives thereof.
6. The pharmaceutical composition of claim 4 or claim 5, wherein the recombinant herpes simplex virus genome has been engineered to reduce or eliminate expression of one or more toxic herpes simplex virus genes.
7. The pharmaceutical composition of any one of claims 4-6, wherein the recombinant herpes simplex virus genome comprises an inactivating mutation in a herpes simplex virus gene selected from the group consisting of Infected Cell Protein (ICP) 0, ICP4, ICP22, ICP27, ICP47, thymidine kinase (tk), Long Unique Region (UL) 41, and UL55.
8. The pharmaceutical composition of claim 7, wherein the recombinant herpes simplex virus genome comprises an inactivating mutation in one or both copies of the ICP4 gene and/or an inactivating mutation in the ICP22 gene.

9. The pharmaceutical composition of any one of claims 4-8, wherein the recombinant herpes simplex virus genome comprises the one or more polynucleotides encoding the CFTR polypeptide within one or both of the ICP4 viral gene loci, within the ICP22 viral gene locus, within the UL41 viral gene locus, within one or both of the ICP0 viral gene loci, within the ICP27 viral gene locus, within the ICP47 viral gene locus, and/or within the UL55 viral gene locus.
10. The pharmaceutical composition of any one of claims 1-9, wherein the recombinant herpes virus genome has reduced cytotoxicity when introduced into a target cell as compared to a corresponding wild-type herpes virus genome.
11. The pharmaceutical composition of any one of claims 1-10, wherein the pharmaceutical composition is formulated for administration to a subject in need thereof using in a nebulizer.
12. The pharmaceutical composition of claim 11, wherein the nebulizer is a jet nebulizer, an ultrasonic nebulizer, or a vibrating mesh nebulizer.
13. The pharmaceutical composition of any one of claims 1-12, wherein the pharmaceutical composition comprises a phosphate buffer, glycerol, a lipid carrier, and/or a nanoparticle carrier.
14. The pharmaceutical composition of any one of claims 1-13, wherein the pharmaceutical composition is aerosolized via nebulization.
15. The pharmaceutical composition of claim 14, wherein the aerosolized pharmaceutical composition comprises droplets having diameters less than about 5 microns mass median aerodynamic diameter.
16. Use of the pharmaceutical composition of any one of claims 1-15 in the manufacture of a medicament for enhancing, increasing, augmenting, and/or supplementing the levels of a CFTR polypeptide in one or more cells of a subject in need thereof.
17. Use of the pharmaceutical composition of any one of claims 1-15 in the manufacture of a medicament for reducing or inhibiting progressive lung destruction in a subject in need thereof.
18. Use of the pharmaceutical composition of any one of claims 1-15 in the manufacture of a medicament for providing prophylactic, palliative, or therapeutic relief of one or more signs or symptoms of a chronic lung disease in a subject in need thereof.
19. The use of claim 18, wherein the chronic lung disease is cystic fibrosis or chronic obstructive pulmonary disease (COPD).

20. The use of any one of claims 16-19, wherein the subject is a human and/or the subject's genome comprises a loss-of-function mutation in a *CFTR* gene.
21. The use of any one of claims 16-20, wherein the medicament is formulated for administration to the subject using a nebulizer.
22. A kit, comprising:
a pharmaceutical composition comprising (a) a herpes virus comprising a recombinant herpes virus genome, wherein the recombinant herpes virus genome comprises one or more polynucleotides encoding a cystic fibrosis transmembrane conductance regulator (CFTR) polypeptide; and (b) a pharmaceutically acceptable excipient; and
a nebulizer.
23. The kit of claim 22, further comprising instructions for administering the pharmaceutical composition using the nebulizer to the lungs of a subject suffering from cystic fibrosis or chronic obstructive pulmonary disease (COPD).
24. A nebulizer containing a pharmaceutical composition comprising (a) a herpes virus comprising a recombinant herpes virus genome, wherein the recombinant herpes virus genome comprises one or more polynucleotides encoding a cystic fibrosis transmembrane conductance regulator (CFTR) polypeptide; and (b) a pharmaceutically acceptable excipient.
25. The nebulizer of claim 24, wherein the pharmaceutical composition is a liquid formulation.