CLAIMS

~~**WHAT IS CLAIMED IS:**~~

1. An isolated polynucleotide comprising a nucleotide sequence having at least 95% sequence identity to the nucleotide sequence of SEQ ID NO:1.

2. The isolated polynucleotide of claim 1, comprising a nucleotide sequence having at least 96%, at least 97%, at least 98%, or at least 99% sequence identity to the nucleotide sequence of SEQ ID NO:1.

3. The isolated polynucleotide of claim 1 or 2, comprising the nucleotide sequence of SEQ ID NO:1.

4. An isolated polynucleotide comprising the nucleotide sequence of SEQ ID NO:2.

5. An isolated polynucleotide comprising a nucleotide sequence having at least 95% sequence identity to the nucleotide sequence of SEQ ID NO:3.

6. The isolated polynucleotide of claim 5, comprising a nucleotide sequence having at least 96%, at least 97%, at least 98%, or at least 99% sequence identity to the nucleotide sequence of SEQ ID NO:3.

7. The isolated polynucleotide of claim 5 or 6, comprising the nucleotide sequence of SEQ ID NO:3.

8. A lentiviral transfer vector comprising a promoter operably linked to a codon-optimized human CFTR gene, wherein expression of the codon-optimized human CFTR gene in cystic fibrosis human airway epithelial cells results in an increase in transepithelial Cl^- transport compared to wild-type human CFTR.

9. A lentiviral transfer vector comprising a promoter operably linked to the polynucleotide of any one of claims 1-7.

10. The lentiviral transfer vector of claim 9, wherein the promoter is a human phosphoglycerate kinase promoter (PGK).

11. The lentiviral transfer vector of claim 10, wherein the PGK promoter has at least 95% sequence identity to the nucleotide sequence of SEQ ID NO:4.

12. The lentiviral transfer vector of claim 9, wherein the promoter is a human elongation factor 1-α (EF1α) promoter.

13. A lentiviral transfer vector comprising an EF1α promoter operably linked to a human

CFTR gene.

14. The lentiviral transfer vector of claim 12 or claim 13, wherein the EF1α promoter has at least 95% sequence identity to the nucleotide sequence of SEQ ID NO:5.

15. A lentiviral transfer vector comprising a promoter operably linked to a polynucleotide comprising a nucleotide sequence having at least 95% sequence identity to the nucleotide sequence of SEQ ID NO:2.

16. The lentiviral vector of any one of claims 8 to 15, wherein the lentiviral components of the lentiviral vector originate from HIV-1.

17. The lentiviral vector of any one of claims 8 to 16, further comprising one or more of a 5' long terminal repeat (LTR), a 3' LTR, a packaging signal, a Rev response element (RRE), a central polypurine tract (cPPT) sequence, and/or a central termination sequence (CTS).

18. The lentiviral vector of claim 17, wherein the 3' LTR is a self-inactivating 3' LTR.

19. The lentiviral vector of claim 17 or 18, wherein the 3' LTR comprises an insertion of a human ankyrin 1 element in the reverse orientation.

20. The lentiviral vector of any one of claims 17 to 19, wherein the 3' LTR comprises a polynucleotide sequence having at least 95% sequence identity to the nucleotide sequence of SEQ ID NO:13.

21. The lentiviral vector of claim 20, wherein the 3' LTR comprises the polynucleotide sequence of SEQ ID NO:13.

22. A virion comprising the lentiviral vector of any one of claims 8-21.

23. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and the isolated polynucleotide of any one of claims 1 to 7, the lentiviral vector of any one of claims 8 to 21, or the virion of claim 22.

24. Use of the isolated polynucleotide of any one of claims 1 to 7, the lentiviral vector of any one of claims 8 to 21, the virion of claim 22, or the pharmaceutical composition of claim 23 in the manufacture of a medicament for~~A method of treating~~ the treatment of cystic fibrosis~~, the method comprising administering to a subject in need thereof a therapeutically effective amount of the isolated polynucleotide of any one of claims 1 to 7, the lentiviral vector of any one of claims 8 to 21, the virion of claim 22, or the pharmaceutical composition of claim 23~~.

25. The use~~method~~ of claim 24, ~~further comprising administering~~wherein the medicament is to be administered with one or more additional therapeutic agents ~~to the subject~~.

26. The use~~method~~ of claim 25, wherein the one or more additional therapeutic agents includes an antibiotic, a mucus thinner, a CFTR modulator, a mucolytic, normal saline, hypertonic saline, or a combination thereof.

27. The use~~method~~ of any one of claims 24 to 26, wherein the medicament is to be administered ~~administering is~~ by inhalation, nebulization, atomization or via atomizer, or aerosolization, and/or by intranasal, intratracheal, intrabronchial, oral, intravenous, subcutaneous, or intramuscular administration~~intranasally, intratracheally, intrabronchially, orally, intravenously, subcutaneously, or intramuscularly~~.

28. The use~~method~~ of claim 27, wherein the medicament is to be administered~~administering is~~ by inhalation, nebulization, atomization or via atomizer, or aerosolization, and/or by intranasal, intratracheal, or intrabronchial administration~~intranasally, intratracheally, and/or intrabronchially~~.

29. The polynucleotide of any one of claims 1 to 7, the lentiviral vector of any one of claims 8 to 21, the virion of claim 22, or the pharmaceutical composition of claim 23 for use in ~~treating~~ the treatment of cystic fibrosis.

30. The polynucleotide, lentiviral vector, virion, or pharmaceutical composition for use of claim 29, which is administered in combination with one or more additional therapeutic agents.

31. The polynucleotide, lentiviral vector, virion, or pharmaceutical composition for use of claim 30, wherein the one or more additional therapeutic agents includes an antibiotic, a mucus thinner, a CFTR modulator, a mucolytic, normal saline, hypertonic saline, or a combination thereof.

32. The polynucleotide, lentiviral vector, virion, or pharmaceutical composition for use of claim 30 or 31, which is to be administered by inhalation, nebulization, atomization or via atomizer, or aerosolization, and/or by intranasal, intratracheal, intrabronchial, oral, intravenous, subcutaneous, or intramuscular administration~~intranasally, intratracheally, intrabronchially, orally, intravenously, subcutaneously, or intramuscularly~~.

33. The polynucleotide, lentiviral vector, virion, or pharmaceutical composition for use of claim 32, which is to be administered by inhalation, nebulization, atomization or via atomizer, or aerosolization, and/or by intranasal, intratracheal, or intrabronchial administration~~intranasally, intratracheally, and/or intrabronchially~~.

34. An atomizer sprayer or nebulizer comprising the isolated polynucleotide of any one of claims 1 to 7, the lentiviral vector of any one of claims 8 to 21, the virion of claim 22, or the pharmaceutical composition of claim 23.