CLAIMS

1. A recombinant adeno-associated virus (rAAV) comprising (i) an AV.TL65 capsid protein, the AV.TL65 capsid protein having at least 80% amino acid sequence identity to SEQ ID NO:13; and (ii) a polynucleotide comprising an F5 enhancer, the F5 enhancer having at least 80% nucleic acid sequence identity to SEQ ID NO:14, and a tg83 promoter, the tg83 promoter having at least 80% nucleic acid sequence identity to SEQ ID NO:2, operably linked to a CFTRΔR minigene.

2. The rAAV of claim 1, wherein the AV.TL65 capsid protein has at least 95% amino acid sequence identity to SEQ ID NO:13.

3. The rAAV of claim 2, wherein the AV.TL65 capsid protein has at least 99% amino acid sequence identity to SEQ ID NO:13.

4. The rAAV of claim 3, wherein the AV.TL65 capsid protein comprises the amino acid sequence of SEQ ID NO:13.

5. The rAAV of any one of claims 1 to 4, wherein the F5 enhancer comprises the polynucleotide sequence of SEQ ID NO:1.

6. The rAAV of any one of claims 1 to 4, wherein the F5 enhancer has at least 95% nucleic acid sequence identity to SEQ ID NO:14.

7. The rAAV of claim 6, wherein the F5 enhancer has at least 99% nucleic acid sequence identity to SEQ ID NO:14.

8. The rAAV of claim 7, wherein the F5 enhancer comprises the polynucleotide sequence of SEQ ID NO:14.

9. The rAAV of any one of claims 1 to 8, wherein the tg83 promoter has at least 95% nucleic acid sequence identity to SEQ ID NO:2.

10. The rAAV of claim 9, wherein the tg83 promoter has at least 99% nucleic acid sequence identity to SEQ ID NO:2.

11. The rAAV of claim 10, wherein the tg83 promoter comprises the polynucleotide sequence of SEQ ID NO:2.

12. The rAAV of any one of claims 1 to 11, wherein the CFTRΔR minigene is a human CFTRΔR minigene.

13. The rAAV of claim 12, wherein the human CFTRΔR minigene is encoded by a polynucleotide having at least 80% nucleic acid sequence identity to SEQ ID NO:4.

14. The rAAV of claim 13, wherein the human CFTRΔR minigene is encoded by a polynucleotide having at least 95% nucleic acid sequence identity to SEQ ID NO:4.

15. The rAAV of claim 14, wherein the human CFTRΔR minigene is encoded by a polynucleotide having at least 99% nucleic acid sequence identity to SEQ ID NO:4.

16. The rAAV of claim 15, wherein the human CFTRΔR minigene is encoded by a polynucleotide comprising the nucleic acid sequence of SEQ ID NO:4.

17. The rAAV of any one of claims 1 to 16, wherein the polynucleotide comprises, in a 5'-to-3' direction, the F5 enhancer, the tg83 promoter, and the CFTRΔR minigene.

18. The rAAV of any one of claims 1 to 17, wherein the polynucleotide comprises, in a 5'-to-3' direction, the AV.TL65 capsid protein comprising the amino acid sequence of SEQ ID NO:13, the F5 enhancer comprising the polynucleotide sequence of SEQ ID NO:14, the tg83 promoter comprising the polynucleotide sequence of SEQ ID NO:2, and the human CFTRΔR minigene encoded by a polynucleotide comprising the nucleic acid sequence of SEQ ID NO:4.

19. An rAAV comprising, in a 5'-to-3' direction, (i) an AV.TL65 capsid protein comprising the amino acid sequence of SEQ ID NO:13; and (ii) an isolated polynucleotide comprising the sequence of SEQ ID NO:7.

20. A pharmaceutical composition comprising the rAAV of any one of claims 1 to 19 and a pharmaceutically acceptable carrier.

21. Use of the rAAV of any one of claims 1 to 19 or the pharmaceutical composition of claim 20 in the manufacture of a medicament for treating cystic fibrosis.

22. The use of claim 21, wherein the medicament is formulated for administration in combination with one or more additional therapeutic agents.

23. The use of claim 22, wherein the one or more additional therapeutic agents includes an antibiotic, a mucus thinner, a CFTR modulator, a mucolytic, normal saline, hypertonic saline, an immunosuppressive agent, or a combination thereof.

24. The use of any one of claims 21 to 23, wherein the medicament is formulated for administration by inhalation, by nebulization, or by aerosolization, or by intranasal, intratracheal, intrabronchial, oral, intravenous, subcutaneous, or intramuscular administration.

25. The use of claim 24, wherein the medicament is formulated for administration by inhalation, by nebulization, or by aerosolization, or by intranasal, intratracheal, and/or intrabronchial administration.

26. The rAAV of any one of claims 1-19 or the pharmaceutical composition of claim 20 for use in treating cystic fibrosis.

27. The rAAV for use or the pharmaceutical composition for use of claim 26, wherein the rAAV or the pharmaceutical composition is formulated for administration in combination with one or more additional therapeutic agents.

28. The rAAV for use or the pharmaceutical composition for use of claim 27, wherein the one or more additional therapeutic agents includes an antibiotic, a mucus thinner, a CFTR modulator, a mucolytic, normal saline, hypertonic saline, an immunosuppressive agent, or a combination thereof.

29. The rAAV for use or the pharmaceutical composition for use of any one of claims 26 to 28, wherein the rAAV or the pharmaceutical composition is formulated for administration by inhalation, by nebulization, or by aerosolization, or by intranasal, intratracheal, intrabronchial, oral, intravenous, subcutaneous, or intramuscular administration.

30. The rAAV for use or the pharmaceutical composition for use of claim 29, wherein the rAAV or the pharmaceutical composition is formulated for administration by inhalation, by nebulization, or by aerosolization, or by intranasal, intratracheal, and/or intrabronchial administration.

31. The rAAV of claim 19, further comprising, in the 3’ direction, a 3’ untranslated region (3’-UTR) comprising the sequence of SEQ ID NO:5.

32. The rAAV of claim 19 or 31 further comprising, in the 3’ direction, a synthetic polyadenylation site comprising the sequence of SEQ ID NO:6.

33. The rAAV of any one of claims 19, 31, and 32, further comprising a 5’ adeno-associated virus (AAV) inverted terminal repeat at the 5’ terminus of the polynucleotide and a 3’ AAV ITR at the 3’ terminus of the polynucleotide.

34. The rAAV of claim 33, wherein the polynucleotide comprises the sequence of SEQ ID NO:17.