We claim:

1. A recombinant adeno-associated virus vector (rAAV) comprising a codon-optimized sequence encoding a human phenylalanine hydroxylase (PAH), wherein the codon-optimized sequence has at least 70% identity to one of SEQ ID Nos: 11-27.

2. The rAAV of claim 1, wherein the codon-optimized sequence has at least 75%, 80%, 85%, 90%, 95% or 99% identity to one of SEQ ID Nos: 11-27.

3. The rAAV of claim 1 or 2, wherein the codon-optimized sequence is identical to one of SEQ ID Nos: 11-27.

4. The rAAV of any one of the preceding claims, wherein the rAAV encodes an AAV8 capsid.

5. The rAAV of claim 4, wherein the AAV8 capsid is a modified AAV8 capsid with improved liver tropism compared to the wild-type AAV8 capsid.

6. The rAAV of claim 5, wherein the AAV8 capsid has at least 70%, 75%, 80%, 85%, 90%, 95% or 99% identity to the wild-type AAV8 capsid.

7. The rAAV of any one of the preceding claims, wherein the rAAV further comprises a WPRE sequence.

8. The rAAV of claim 7, wherein the WPRE sequence is a naturally-occurring WPRE sequence.

9. The rAAV of claim 7, wherein the WPRE sequence is a modified WPRE sequence.

10. The rAAV of claim of any one of the preceding claims, wherein the rAAV further comprises a liver-specific promoter.

11. The rAAV of claim 10, wherein the liver-specific promoter is a transthyretin promotor (TTR).

12. The rAAV of any one of the preceding claims, wherein the rAAV comprises a cis-acting regulatory module (CRM).

13. The rAAV of claim 12, wherein the vector comprises one, two, three, four, five or more CRM repeats.

14. The rAAV of claim 12 or 13, wherein the CRM is CRM8.

15. The rAAV of any one of the preceding claims, wherein the rAAV further comprises an intron upstream of the PAH sequence.

16. The rAAV of claim 15, wherein the intron is a minute virus of mice (MVM) intron.

17. A method of treating phenylketonuria (PKU), comprising administering to a subject in need of treatment a recombinant adeno-associated virus (rAAV) comprising
a codon-optimized sequence encoding a human phenylalanine hydroxylase (PAH), wherein the codon-optimized sequence has at least 70% identity to one of SEQ ID Nos: 11-27.

18. The method of claim 17, wherein administering the rAAV results in a decrease in plasma phenylalanine (Phe) level in the subject compared to a control.

19. The method of claim 17 or 18, wherein administering the rAAV results in an increase in plasma tyrosine level in the subject compared to a control.

20. The method of any one of claims 17-19, wherein administering the rAAV results in an increase in plasma tryptophan level in the subject compared to a control.

21. The method of any one of claims 18-20, wherein the control is the pre-treatment level in the subject.

22. The method of any one of claims 18-20, wherein the control is a reference level based on historical data.

23. The method of any one of claims 17-22, wherein the codon-optimized sequence has at least 75%, 80%, 85%, 90%, 95% or 99% identity to one of SEQ ID Nos: 11-27.

24. The method of any one of claims 17-23, wherein the codon-optimized sequence is identical to one of SEQ ID Nos: 11-27.

25. The method of any one of claims 17-24, wherein the rAAV encodes an AAV8 capsid.

26. The method of claim 25, wherein the AAV8 capsid is a modified AAV8 capsid with improved liver tropism compared to the wild-type AAV8 capsid.

27. The method of claim 25, wherein the AAV8 capsid has at least 70%, 75%, 80%, 85%, 90%, 95% or 99% identity to the wild-type AAV capsid.

28. The method of any one of claims 17-27, wherein the rAAV further comprises a WPRE sequence.

29. The method of claim 28, wherein the WPRE sequence is a naturally-occurring WPRE sequence.

30. The method of claim 28, wherein the WPRE sequence is a modified WPRE sequence.

31. The method of any one of claims 17-30, wherein the rAAV further comprises a liver-specific promoter.

32. The method of claim 31, wherein the liver-specific promoter is a transthyretin promotor (TTR).

33. The method of any one of claims 17-32, wherein the rAAV comprises a cis-acting regulatory module (CRM).

34. The method of claim 33, wherein the vector comprises one, two, three, four, five or more CRM repeats.

35. The method of claim 33 or 34, wherein the CRM is CRM8.

36. The method of any one of claims 17-35, wherein the rAAV further comprises an intron upstream of the PAH sequence.

37. The method of claim 36, wherein the intron is a minute virus of mice (MVM) intron.

38. The method of any one of claims 17-37, wherein the rAAV is administered at dose of about $1x10^{10}$ vg/kg, about $1x10^{11}$ vg/kg, about $1x10^{12}$ vg/kg, about $1x10^{13}$ vg/kg, about $1x10^{14}$ vg/kg, or about $1x10^{15}$ vg/kg.

39. The method of any one of claims 17-38, wherein the rAAV is administered systemically.

40. The method of any one of claims 17-38, wherein the rAAV is administered intravenously.