CLAIMS

WHAT IS CLAIMED IS:

1. An engineered polynucleotide comprising an AAV vector, said AAV vector comprises an expression cassette, wherein the expression cassette encodes an engineered polypeptide comprising a natriuretic peptide covalently connected to an antibody or fragment thereof.

2. The engineered polynucleotide of claim 1, wherein the natriuretic peptide comprises an amino acid sequence that is at least 80%, at least 90%, at least 95%, or at least 99% identical to any one of **SEQ ID NOs: 1-5**.

3. The engineered polynucleotide of claim 1, wherein the natriuretic peptide comprises an amino acid sequence that is at least 80%, at least 90%, at least 95%, or at least 99% identical to **SEQ ID NO: 4**.

4. The engineered polynucleotide of claim 1, wherein the antibody or fragment thereof comprises a fragment crystallizable (Fc) region.

5. The engineered polynucleotide of claim 1, wherein the antibody or fragment thereof comprises an amino acid sequence that is at least 80%, at least 90%, at least 95%, or at least 99% identical to any one of **SEQ ID NOs: 6-8**.

6. The engineered polynucleotide of claim 1, wherein the natriuretic peptide is covalently connected to the antibody or fragment thereof by a peptide linker.

7. The engineered polynucleotide of claim 1, wherein the engineered polypeptide comprises a protease cleavage site.

8. The engineered polynucleotide of claim 7, wherein the proteases cleavage site comprises a Furin protease site.

9. The engineered polynucleotide of claim 1, wherein the engineered polypeptide comprises an amino acid sequence that is at least 80%, at least 90%, at least 95%, or at least 99% identical to any one of **SEQ ID NOs: 131-140**.

10. The engineered polynucleotide of claim 1, wherein the natriuretic peptide comprises a C-type natriuretic peptide (CNP) or fragment thereof.

11. The engineered polynucleotide of claim 1, the AAV vector comprises an AAV serotype comprising AAV1, AAV2, AAV3, AAV4, AAV5, AAV6, AAV7, AAV8, AAV9, AAV10, AAV11, AAV12, or any combination thereof.

12. The engineered polynucleotide of claim 11, wherein the AAV serotype comprises the AAV2.

13. The engineered polynucleotide of claim 1, wherein the AAV vector encodes an modified AAV capsid.

14. The engineered polynucleotide of claim 1, wherein the AAV vector comprises a second expression cassette for encoding a therapeutic.

15. The engineered polynucleotide of claim 14, wherein the therapeutic comprises a hormone, an agonist of a natriuretic peptide receptor (NPR), an agonist of a cyclic GMP (cGMP) signaling pathway, or an VEGF inhibitor.

16. A pharmaceutical composition comprising the engineered polynucleotide of claim 1.

17. The pharmaceutical composition of claim 16, wherein pharmaceutical composition is formulated for administering intrathecally, intraocularly, intravitreally, retinally, intravenously, intramuscularly, intraventricularly, intracerebrally, intracerebellarly, intracerebroventricularly, intraperenchymally, subcutaneously, subretinally, suprachoroidally, intratumorally, pulmonarily, endotracheally, intraperitoneally, intravesically, intravaginally, intrarectally, orally, sublingually, transdermally, by inhalation, by inhaled nebulized form, by intraluminal-GI route, or a combination thereof to a subject in need thereof.

18. The pharmaceutical composition of claim 17, wherein the pharmaceutical composition is for treating an ocular disease or condition.

19. Use of an engineered polynucleotide in the manufacture of a medicament for treating a disease or condition in a subject, wherein the engineered polynucleotide is to be administered to the subject, wherein the engineered polynucleotide comprises a viral vector comprising an expression cassette for expressing an engineered polypeptide comprising an antibody or a fragment thereof operatively coupled to a natriuretic peptide in a cell of the subject, and wherein the cell expresses the engineered polypeptide.

20. The use of claim 19, wherein the disease or condition comprises an ocular disease.