WHAT IS CLAIMED IS:

1. A recombinant oncolytic adenovirus comprising a first nucleotide sequence encoding a first therapeutic transgene selected from human endostatin and human angiostatin inserted ~~into an E1b-19K insertion site, wherein the E1b-19K insertion site is located~~ between the start codon~~site~~ of E1b-19K and the start codon~~site~~ of E1b-55K.

2. The recombinant oncolytic adenovirus of claim 1, wherein the recombinant oncolytic adenovirus is a type 5 adenovirus (Ad5).

~~3. The recombinant adenovirus of claim 1 or 2, wherein the E1b-19K insertion site is located between the start site of E1b-19K and the stop site of E1b-19K.~~

~~4. The recombinant adenovirus of any one of claims 1-3, wherein the E1b-19K insertion site comprises a deletion of from about 100 to about 305, about 100 to about 300, about 100 to about 250, about 100 to about 200, about 100 to about 150, about 150 to about 305, about 150 to about 300, about 150 to about 250, or about 150 to about 200 nucleotides adjacent the start site of E1b-19K.~~

~~5. The recombinant adenovirus of any one of claims 1-4, wherein the E1b-19K insertion site comprises a deletion of about 200 nucleotides adjacent the start site of E1b-19K.~~

~~6. The recombinant adenovirus of any one of claims 1-5, wherein the E1b-19K insertion site comprises a deletion of 202 nucleotides adjacent the start site of E1b-19K.~~

~~7. The recombinant adenovirus of any one of claims 1-5, wherein the E1b-19K insertion site comprises a deletion of 203 nucleotides adjacent the start site of E1b-19K.~~

~~8. The recombinant adenovirus of any one of claims 1-7, wherein the E1b-19K insertion site comprises a deletion corresponding to nucleotides 1714-1916 of the Ad5 genome (SEQ ID NO: 1).~~

~~9. The recombinant adenovirus of any one of claims 1-8, wherein the first therapeutic transgene is inserted between nucleotides corresponding to 1713 and 1917 of the Ad5 genome (SEQ ID NO: 1).~~

~~10. The recombinant adenovirus of any one of claims 1-9, wherein the first therapeutic transgene is inserted between CTGACCTC (SEQ ID NO: 2) and TCACCAGG (SEQ ID NO: 3).~~

~~11. The recombinant adenovirus of any one of claims 1-10, wherein the recombinant adenovirus comprises, in a 5' to 3' orientation, CTGACCTC (SEQ ID NO: 2), the first therapeutic transgene, and TCACCAGG (SEQ ID NO: 3).~~

3~~12~~. The recombinant oncolytic adenovirus of ~~any one of~~ claim~~s~~ 1 or claim 2~~-11~~, wherein the recombinant oncolytic adenovirus comprises a second nucleotide sequence encoding a second therapeutic transgene selected from human endostatin and human angiostatin, wherein the first therapeutic transgene and the second therapeutic transgene do not express the same protein.

~~13. The recombinant adenovirus of claim 12, wherein the second therapeutic transgene is inserted into the E1b-19k insertion site, and the first nucleotide sequence and the second nucleotide sequence are separated by an internal ribosome entry site (IRES).~~

~~14. The recombinant adenovirus of claim 13, wherein the IRES is selected from an encephalomyocarditis virus IRES, a foot-and-mouth disease virus IRES, and a poliovirus IRES.~~

~~15. The recombinant adenovirus of claim 14, wherein the IRES is an encephalomyocarditis virus IRES.~~

~~16. The recombinant adenovirus of claim 15, wherein the IRES comprises SEQ ID NO: 20.~~

~~17. The recombinant adenovirus of any one of claims 13-16, wherein the first and second therapeutic transgenes are inserted between nucleotides corresponding to 1713 and 1917 of the Ad5 genome (SEQ ID NO: 1).~~

~~18. The recombinant adenovirus of any one of claims 13-17, wherein the first and second therapeutic transgenes are inserted between CTGACCTC (SEQ ID NO: 2) and TCACCAGG (SEQ ID NO: 3).~~

~~19. The recombinant adenovirus of any one of claims 13-18, wherein the recombinant adenovirus comprises, in a 5' to 3' orientation, CTGACCTC (SEQ ID NO: 2), the first therapeutic transgene, the IRES, the second therapeutic transgene, and TCACCAGG (SEQ ID NO: 3).~~

4~~20~~. The recombinant oncolytic adenovirus of any one of claims 1-3~~19~~, wherein the recombinant oncolytic adenovirus further comprises an E3 deletion.~~,~~

5. The recombinant oncolytic adenovirus of claim 3, wherein the second therapeutic transgene ~~E3 deletion~~ is ~~located~~inserted between the stop codon~~site~~ of pVIII and the start codon~~site~~ of Fiber.

~~21. The recombinant adenovirus of claim 20, wherein the E3 deletion is located between the stop site of E3-10.5K and the stop site of E3-14.7K.~~

~~22. The recombinant adenovirus of claim 20 or 21, wherein the E3 deletion comprises a deletion of from about 500 to about 3185, from about 500 to about 3000, from about 500 to about 2500, from about 500 to about 2000, from about 500 to about 1500, from about 500 to about 1000, from about 1000 to about 3185, from about 1000 to about 3000, from about 1000 to about 2500, from about 1000 to about 2000, from about 1000 to about 1500, from about 1500 to about 3185, from about 1500 to about 3000, from about 1500 to about 2000, from about 2000 to about 3185, from about 2000 to about 3000, from about 2000 to about 2500, from about 2500 to about 3185, from about 2500 to about 3000, or from about 3000 to about 3185 nucleotides.~~

~~23. The recombinant adenovirus of any one of claims 20-22, wherein the E3 deletion comprises a deletion of from about 500 to about 1551, from about 500 to about 1500, from about 500 to about 1000, from about 1000 to about 1551, from about 1000 to about 1500, or from about 1500 to about 1551 nucleotides adjacent the stop site of E3-10.5K.~~

~~24. The recombinant adenovirus of any one of claims 20-23, wherein the E3 deletion comprises a deletion of about 1050 nucleotides adjacent the stop site of E3-10.5K.~~

~~25. The recombinant adenovirus of any one of claims 20-24, wherein the E3 deletion comprises a deletion of 1063 nucleotides adjacent the stop site of E3-10.5K.~~

~~26. The recombinant adenovirus of any one of claims 20-24, wherein the E3 deletion comprises a deletion of 1064 nucleotides adjacent the stop site of E3-10.5K.~~

~~27. The recombinant adenovirus of any one of claims 20-26, wherein the E3 deletion comprises a deletion corresponding to the Ad5 dl309 E3 deletion.~~

~~28. The recombinant adenovirus of any one of claims 20-27, wherein the E3 deletion comprises a deletion corresponding to nucleotides 29773-30836 of the Ad5 genome (SEQ ID NO: 1).~~

~~29. The recombinant adenovirus of claim 12, wherein the second therapeutic transgene is inserted into an E3 insertion site, wherein the E3 insertion site is located between the stop site of pVIII and the start site of Fiber.~~

~~30. The recombinant adenovirus of claim 29, wherein the E3 insertion site is located between the stop site of E3-10.5K and the stop site of E3-14.7K.~~

~~31. The recombinant adenovirus of claim 29 or 30, wherein the E3 insertion site comprises a deletion of from about 500 to about 3185, from about 500 to about 3000, from about 500 to about 2500, from about 500 to about 2000, from about 500 to about 1500, from about 500 to about 1000, from about 1000 to about 3185, from about 1000 to about 3000, from about 1000 to about 2500, from about 1000 to about 2000, from about 1000 to about 1500, from about 1500 to about 3185, from about 1500 to about 3000, from about 1500 to about 2000, from about 2000 to about 3185, from about 2000 to about 3000, from about 2000 to about 2500, from about 2500 to about 3185, from about 2500 to about 3000, or from about 3000 to about 3185 nucleotides.~~

~~32. The recombinant adenovirus of any one of claims 29-31, wherein the E3 insertion site comprises a deletion of from about 500 to about 1551, from about 500 to about 1500, from about 500 to about 1000, from about 1000 to about 1551, from about 1000 to about 1500, or from about 1500 to about 1551 nucleotides adjacent the stop site of E3-10.5K.~~

~~33. The recombinant adenovirus of any one of claims 29-32, wherein the E3 insertion site comprises a deletion of about 1050 nucleotides adjacent the stop site of E3-10.5K.~~

~~34. The recombinant adenovirus of any one of claims 29-33, wherein the E3 insertion site comprises a deletion of 1063 nucleotides adjacent the stop site of E3-10.5K.~~

~~35. The recombinant adenovirus of any one of claims 29-34, wherein the E3 insertion site comprises a deletion of 1064 nucleotides adjacent the stop site of E3-10.5K.~~

~~36. The recombinant adenovirus of any one of claims 29-35, wherein the E3 insertion site comprises a deletion corresponding to the Ad5 dl309 E3 deletion.~~

~~37. The recombinant adenovirus of any one of claims 29-36, wherein the E3 insertion site comprises a deletion corresponding to nucleotides 29773-30836 of the Ad5 genome (SEQ ID NO: 1).~~

~~38. The recombinant adenovirus of any one of claims 29-37, wherein the second therapeutic transgene is inserted between nucleotides corresponding to 29773 and 30836 of the Ad5 genome (SEQ ID NO: 1).~~

~~39. The recombinant adenovirus of any one of claims 29-38, wherein the second therapeutic transgene is inserted between CAGTATGA (SEQ ID NO: 4) and TAATAAAAAA (SEQ ID NO: 5).~~

~~40. The recombinant adenovirus of any one of claims 29-39, wherein the recombinant adenovirus comprises, in a 5' to 3' orientation, CAGTATGA (SEQ ID NO: 4), the second therapeutic transgene, and TAATAAAAAA (SEQ ID NO: 5).~~

6~~41~~. The recombinant oncolytic adenovirus of any one of claims 1-5~~40~~, wherein the recombinant oncolytic adenovirus comprises a nucleotide sequence encoding an~~the~~ amino acid sequence having 95% sequence identity to ~~of~~ SEQ ID NO: 7, a nucleotide sequence encoding an amino acid sequence having 95% sequence identity to SEQ ID NO: 8, a nucleotide sequence having 95% sequence identity to SEQ ID NO: 9, a nucleotide sequence encoding an amino acid sequence having 95% sequence identity to an amino acid sequence selected from SEQ ID NO: 12, SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15, and SEQ ID NO: 16, a nucleotide sequence encoding an amino acid sequence having 95% sequence identity to SEQ ID NO: 17, or a nucleotide sequence having 95% sequence identity to SEQ ID NO: 18~~or a nucleotide sequence encoding an amino acid sequence having 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to SEQ ID NO: 7~~.

~~42. The recombinant adenovirus of any one of claims 1-41, wherein the recombinant adenovirus comprises a nucleotide sequence encoding the amino acid sequence of SEQ ID NO: 8, or a nucleotide sequence encoding an amino acid sequence having 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to SEQ ID NO: 8.~~

~~43. The recombinant adenovirus of any one of claims 1-42, wherein the recombinant adenovirus comprises the nucleotide sequence of SEQ ID NO: 9, or comprises a sequence having 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to SEQ ID NO: 9.~~

~~44. The recombinant adenovirus of any one of claims 1-43, wherein the recombinant adenovirus comprises a nucleotide sequence encoding an amino acid sequence selected from SEQ ID NO: 12, SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15, and SEQ ID NO: 16, or a nucleotide sequence encoding an amino acid sequence having 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to an amino acid sequence selected from SEQ ID NO: 12, SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15, and SEQ ID NO: 16.~~

~~45. The recombinant adenovirus of any one of claims 1-44, wherein the recombinant adenovirus comprises a nucleotide sequence encoding the amino acid sequence of SEQ ID NO: 17, or a nucleotide sequence encoding an amino acid sequence having 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to SEQ ID NO: 17.~~

~~46. The recombinant adenovirus of any one of claims 1-45, wherein the recombinant adenovirus comprises the nucleotide sequence of SEQ ID NO: 18, or comprises a sequence having 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to SEQ ID NO: 18.~~

7~~47~~. The recombinant oncolytic adenovirus of any one of claims 1-6~~46~~, wherein the first and/or second therapeutic transgenes are not operably linked to an exogenous promoter sequence or~~.~~

~~48. The recombinant adenovirus of claim 47,~~ wherein neither of the therapeutic transgenes are operably linked to an exogenous promoter sequence.

8~~49~~. The recombinant oncolytic adenovirus of any one of claims 1-7~~48~~, wherein the recombinant oncolytic adenovirus further comprises a deletion of a Pea3 binding site~~, or a functional fragment thereof~~.

~~50. The recombinant adenovirus of claim 49, wherein the recombinant adenovirus comprises a deletion of nucleotides corresponding to about -300 to about -250 upstream of the initiation site of E1a.~~

~~51. The recombinant adenovirus of claim 49 or 50, wherein the recombinant adenovirus comprises a deletion of nucleotides corresponding to -304 to -255 upstream of the initiation site of E1a.~~

~~52. The recombinant adenovirus of claim 49 or 50, wherein the recombinant adenovirus comprises a deletion of nucleotides corresponding to -305 to -255 upstream of the initiation site of E1a.~~

~~53. The recombinant adenovirus of any one of claims 49-52, wherein the recombinant adenovirus comprises a deletion of nucleotides corresponding to 195-244 of the Ad5 genome (SEQ ID NO: 1).~~

~~54. The recombinant adenovirus of any one of claims 49-53, wherein the recombinant adenovirus comprises the sequence GGTGTTTTGG (SEQ ID NO: 22).~~

~~55. The recombinant adenovirus of any one of claims 49-54, wherein the recombinant adenovirus does not comprise a deletion of an E2F binding site.~~

9~~56~~. The recombinant oncolytic adenovirus of any one of claims 1-7~~48~~, wherein the recombinant oncolytic adenovirus further comprises a deletion of a E2F binding site, ~~or a functional fragment thereof.~~

~~57. The recombinant adenovirus of claim 56,~~ wherein the recombinant oncolytic adenovirus does not comprise a deletion of a Pea3 binding site~~, or a functional fragment thereof~~.

10~~58~~. The recombinant oncolytic adenovirus of any one of claims 1-9~~57~~, wherein the recombinant oncolytic adenovirus comprises an E1a promoter having a deletion of a functional TATA box.

~~59. The recombinant adenovirus of claim 58, wherein the deletion comprises a deletion of the entire TATA box.~~

~~60. The recombinant adenovirus of claim 58 or 59, wherein the deletion comprises a deletion of nucleotides corresponding to -27 to -24 of the E1a promoter.~~

~~61. The recombinant adenovirus of any one of claims 58-60, wherein the deletion comprises a deletion of nucleotides corresponding to -31 to -24 of the E1a promoter.~~

~~62. The recombinant adenovirus of any one of claims 58-61, wherein the deletion comprises a deletion of nucleotides corresponding to -44 to +54 of the E1a promoter.~~

~~63. The recombinant adenovirus of any one of claims 58-62, wherein the deletion comprises a deletion of nucleotides corresponding to -146 to +54 of the E1a promoter.~~

~~64. The recombinant adenovirus of any one of claims 58-63, wherein the deletion comprises a deletion of nucleotides corresponding to 472 to 475 of the Ad5 genome (SEQ ID NO: 1).~~

~~65. The recombinant adenovirus of any one of claims 58-64, wherein the deletion comprises a deletion of nucleotides corresponding to 468 to 475 of the Ad5 genome (SEQ ID NO: 1).~~

~~66. The recombinant adenovirus of any one of claims 58-65, wherein the deletion comprises a deletion of nucleotides corresponding to 455 to 552 of the Ad5 genome (SEQ ID NO: 1).~~

~~67. The recombinant adenovirus of any one of claims 58-66, wherein the deletion comprises a deletion of nucleotides corresponding to 353-552 of the Ad5 genome (SEQ ID NO: 1).~~

~~68. The recombinant adenovirus of any one of claims 58-67, wherein the adenovirus comprises a polynucleotide deletion that results in an adenovirus comprising the sequence CTAGGACTG (SEQ ID NO: 23), AGTGCCCG (SEQ ID NO: 30) and/or TATTCCCG (SEQ ID NO: 31).~~

~~69. The recombinant adenovirus of any one of claims 58-68, wherein the E1a promoter comprises the sequence CTAGGACTG (SEQ ID NO: 23).~~

11~~70~~. The recombinant oncolytic adenovirus of any one of claims 1-10~~69~~, wherein the recombinant oncolytic adenovirus comprises an E1a promoter having a deletion of a functional CAAT box.

~~71. The recombinant adenovirus of claim 70, wherein the deletion comprises a deletion of the entire CAAT box.~~

~~72. The recombinant adenovirus of claim 70 or 71, wherein the deletion comprises a deletion of nucleotides corresponding to -76 to -68 of the E1a promoter.~~

~~73. The recombinant adenovirus of any one of claims 70-72, wherein the deletion comprises a deletion of nucleotides corresponding to 423 to 431 of the Ad5 genome (SEQ ID NO: 1).~~

~~74. The recombinant adenovirus of any one of claims 70-73, wherein the adenovirus comprises a polynucleotide deletion that results in an adenovirus comprising the sequence TTCCGTGGCG (SEQ ID NO: 32).~~

~~75. The recombinant adenovirus of any one of claims 1-74, wherein the recombinant adenovirus selectively replicates in a hyperproliferative cell.~~

12~~76~~. The recombinant oncolytic adenovirus of any one of claims 1-11~~75~~, wherein the recombinant oncolytic adenovirus selectively expresses endostatin and/or angiostatin in thea hyperproliferative cell.

~~77. The recombinant adenovirus of claim 75 or 76, wherein the hyperproliferative cell is a cancer cell.~~

~~78. The recombinant adenovirus of any one of claims 1-77, wherein the recombinant adenovirus is an oncolytic adenovirus.~~

1379. A pharmaceutical composition comprising the recombinant oncolytic adenovirus of any one of claims 1-1278 and at least one pharmaceutically acceptable carrier or diluent.

~~80. A method of expressing endostatin and/or angiostatin in a target cell comprising exposing the cell to an effective amount of the recombinant adenovirus of any one of claims 1-78 to express endostatin and/or angiostatin.~~

~~81. A method of inhibiting proliferation of a tumor cell comprising exposing the cell to an effective amount of the recombinant adenovirus of any one of claims 1-78 to inhibit proliferation of the tumor cell.~~

1482. Use of the pharmaceutical composition of claim 13 in the manufacture of a medicament for~~A method of~~ inhibiting growth of a tumor ~~growth~~ or~~in a subject in need thereof, the method comprising administering to the subject to an effective amount of the recombinant adenovirus of any one of claims 1-78 to inhibit growth of the tumor.~~

~~83. A method of~~ treating a cancer in a subject ~~in need thereof, the method comprising administering to the subject an effective amount of the recombinant adenovirus of any one of claims 1-78 to treat the cancer in the subject~~.

1584. Use of the pharmaceutical composition of claim 13 in the manufacture of a medicament for treating cancer in a subject in need thereof, wherein the pharmaceutical composition further comprises ~~The method of claim 83, wherein the recombinant adenovirus is administered in combination with~~ an anti-angiogenic agent.

~~85. The method of claim 83 or 84, wherein the recombinant adenovirus is administered in combination with one or more therapies selected from surgery, radiation, chemotherapy, immunotherapy, hormone therapy, and virotherapy.~~

~~86. A method of treating cancer in a subject in need thereof, the method comprising administering to the subject an effective amount of a combination of (i) a recombinant adenovirus and (ii) an anti-angiogenic agent to treat the cancer in the subject.~~

~~87. The method of claim 86, wherein the recombinant adenovirus is a type 5 adenovirus (Ad5).~~

~~88. The method of claim 86 or 87, wherein the recombinant adenovirus does not comprise a deletion of a Pea3 binding site, or a functional fragment thereof.~~

~~89. The method of any one of claims 86-88, wherein the recombinant adenovirus comprises an E1a promoter having a deletion of a functional TATA box.~~

~~90. The method of claim 89, wherein the deletion comprises a deletion of the entire TATA box.~~

~~91. The method of claim 89 or 90, wherein the deletion comprises a deletion of nucleotides corresponding to -27 to -24 of the E1a promoter.~~

~~92. The method of any one of claims 89-91, wherein the deletion comprises a deletion of nucleotides corresponding to -31 to -24 of the E1a promoter.~~

~~93. The method of any one of claims 89-92, wherein the deletion comprises a deletion of nucleotides corresponding to -44 to +54 of the E1a promoter.~~

~~94. The method of any one of claims 89-93, wherein the deletion comprises a deletion of nucleotides corresponding to -146 to +54 of the E1a promoter.~~

~~95. The method of any one of claims 89-94, wherein the deletion comprises a deletion of nucleotides corresponding to 472 to 475 of the Ad5 genome (SEQ ID NO: 1).~~

~~96. The method of any one of claims 89-95, wherein the deletion comprises a deletion of nucleotides corresponding to 468 to 475 of the Ad5 genome (SEQ ID NO: 1).~~

~~97. The method of any one of claims 89-96, wherein the deletion comprises a deletion of nucleotides corresponding to 455 to 552 of the Ad5 genome (SEQ ID NO: 1).~~

~~98. The method of any one of claims 89-97, wherein the deletion comprises a deletion of nucleotides corresponding to 353-552 of the Ad5 genome (SEQ ID NO: 1).~~

~~99. The method of any one of claims 89-98, wherein the adenovirus comprises a polynucleotide deletion that results in an adenovirus comprising the sequence CTAGGACTG (SEQ ID NO: 23), AGTGCCCG (SEQ ID NO: 30) and/or TATTCCCG (SEQ ID NO: 31).~~

~~100. The method of any one of claims 89-99, wherein the E1a promoter comprises the sequence CTAGGACTG (SEQ ID NO: 23).~~

~~101. The method of any one of claims 86-100, wherein the recombinant adenovirus comprises an E1a promoter having a deletion of a functional CAAT box.~~

~~102. The method of claim 101, wherein the deletion comprises a deletion of the entire CAAT box.~~

~~103. The method of claim 101 or 102, wherein the deletion comprises a deletion of nucleotides corresponding to -76 to -68 of the E1a promoter.~~

~~104. The method of any one of claims 101-103, wherein the deletion comprises a deletion of nucleotides corresponding to 423 to 431 of the Ad5 genome (SEQ ID NO: 1).~~

~~105. The method of any one of claims 101-104, wherein the adenovirus comprises a polynucleotide deletion that results in an adenovirus comprising the sequence TTCCGTGGCG (SEQ ID NO: 32).~~

~~106. The method of any one of claims 86-105, wherein the recombinant adenovirus selectively replicates in a hyperproliferative cell.~~

~~107. The method of any one of claims 86-106, wherein the recombinant adenovirus selectively expresses endostatin and/or angiostatin in a hyperproliferative cell.~~

~~108. The method of claim 106 or 107, wherein the hyperproliferative cell is a cancer cell.~~

~~109. The method of any one of claims 86-108, wherein the recombinant adenovirus is an oncolytic adenovirus.~~

~~110. The method of any one of claims 86-109, wherein the recombinant adenovirus and anti-angiogenic agent are administered in combination with one or more therapies selected from surgery, radiation, chemotherapy, immunotherapy, hormone therapy, and virotherapy.~~

16~~111~~. The use~~method~~ of ~~any one of~~ claim~~s~~ ~~83-110~~15, wherein the cancer is selected (i) from anal cancer, basal cell carcinoma, bladder cancer, bone cancer, brain cancer, breast cancer, carcinoma, cholangiocarcinoma, cervical cancer, colon cancer, colorectal cancer, endometrial cancer, gastroesophageal cancer, gastrointestinal (GI) cancer, gastrointestinal stromal tumor, hepatocellular carcinoma, gynecologic cancer, head and neck cancer, hematologic cancer, kidney cancer, leukemia, liver cancer, lung cancer, lymphoma, melanoma, merkel cell carcinoma, mesothelioma, neuroendocrine cancer, non-small cell lung cancer, ovarian cancer, pancreatic cancer, pediatric cancer, prostate cancer, renal cell carcinoma, sarcoma, skin cancer, small cell lung cancer, squamous cell carcinoma of the skin, stomach cancer, testicular cancer and thyroid cancer, (ii) ~~.~~

~~112. The method of any one of claims 83-111, wherein the cancer is selected~~ from melanoma, squamous cell carcinoma of the skin, basal cell carcinoma, head and neck cancer, breast cancer, anal cancer, cervical cancer, non-small cell lung cancer, mesothelioma, small cell lung cancer, renal cell carcinoma, prostate cancer, gastroesophageal cancer, colorectal cancer, testicular cancer, bladder cancer, ovarian cancer, liver cancer, hepatocellular carcinoma, cholangiocarcinoma, brain and central nervous system cancer, thyroid cancer, endometrial cancer, neuroendocrine cancer, lymphoma ~~(*e.g.*, Hodgkin and non-Hodgkin)~~, leukemia, merkel

cell carcinoma, gastrointestinal stromal tumors, multiple myeloma, uterine cancer, a sarcoma, kidney cancer, ocular cancer, and pancreatic cancer, (iii) .

113. The method of any one of claims 83-110, wherein the cancer is selected from gastroesophageal cancer (*e.g.*, gastric or gastro-esophageal junction adenocarcinoma), non-small cell lung cancer (*e.g.*, metastatic NSCLC), colorectal cancer (*e.g.*, metastatic colorectal cancer), ovarian cancer (*e.g.*, platinum-resistant ovarian cancer), leukemia, cervical cancer, (*e.g.*, late-stage cervical cancer) brain and central nervous system cancer (*e.g.*, glioblastoma), kidney cancer (*e.g.*, renal cell carcinoma), a sarcoma (*e.g.*, rhabdomyosarcoma, osteosarcoma, and Ewing sarcoma), lymphoma (e.g., Hodgkin and non-Hodgkin), ocular cancer (*e.g.*, choroidal melanoma and retinoblastoma), and von Hippel-Lindau disease, or (iv) .

114. The method of any one of claims 83-110, wherein the cancer is selected from brain and central nervous system cancer (*e.g.*, astrocytoma, brain stem glioma, craniopharyngioma, desmoplastic infantile ganglioglioma, ependymoma, high-grade glioma, medulloblastoma, atypical teratoid rhabdoid tumor, neuroblastoma), kidney cancer (*e.g.*, Wilms tumor), ocular cancer (*e.g.*, retinoblastoma), a sarcoma (*e.g.*, rhabdomyosarcoma, osteosarcoma, and Ewing sarcoma), liver cancer (*e.g.*, hepatoblastoma and hepatocellular carcinoma), lymphoma (*e.g.*, Hodgkin and non-Hodgkin), leukemia, and a germ cell tumor.

17115. The usemethod of any one of claims 15 or claim 1684-114, wherein the anti-angiogenic agent is selected from aflibercept, an anti-VEGF antibody (*e.g.*, bevacizumab and ranibizumab), sunitinib, pazopanib, sorafenib, regorafenib, vandetanib, cabozantinib, axitinib, tivozanib, linifanib, pegaptanib, spironolactone, indomethacin, thalidomide, interleukin-12, an anti- FGF antibody, a tyrosine kinase inhibitor, an interferon, suramin, a suramin analog, somatostatin, and a somatostatin analog.

116. The method of any one of claims 84-114, wherein the anti-angiogenic agent is selected from aflibercept, bevacizumab, ranibizumab, sunitinib, pazopanib, sorafenib, regorafenib, vandetanib, cabozantinib, axitinib, tivozanib and linifanib.

117. The method of claim 115 or 116, wherein the anti-angiogenic agent is bevacizumab.

118. The method of claim 117, wherein bevacizumab is administered at a dose of less than about 5mg/kg, *e.g.*, from about 1 mg/kg to about 5 mg/kg.

119. The method of claim 118, wherein the bevacizumab is administered at a dose of about 2.5 mg/kg.

~~120. The method of any one of claims 83-119, wherein the recombinant adenovirus is administered in combination with a second recombinant adenovirus.~~

18~~121~~. The use~~method~~ of any one of claims 15-17~~120~~, wherein the pharmaceutical composition further comprises a second recombinant oncolytic adenovirus, wherein the second recombinant oncolytic adenovirus (i) comprises a nucleotide sequence encoding a polypeptide, or a fragment thereof, selected from acetylcholine, an androgen-receptor, an anti-PD-1 antibody heavy chain and/or light chain, an anti-PD-L1 antibody heavy chain and/or light chain, BORIS/CTCFL, BRAF, CD19, CD20, CD30, CD80, CD86, CD137, CD137L, CD154, CEA, DKK1/Wnt, EGFRvIII, FGF, gp100, Her-2/neu, ICAM, IL-1, IL-3, IL-4, IL-5, IL-6, IL-8, IL-9, IL-17, IL-23A/p19, p40, IL-24, IL-27, IL-27A/p28, IL-27B/EBI3, IL-35, interferon-gamma, KRAS, MAGE, MAGE-A3, MART1, melan-A, mesothelin, MUC-1, NY-ESO-1, Podocalyxin (Podxl), p53, TGF-β, a TGF-β trap, thymidine kinase, and tyrosinase, ~~.~~

~~122. The method of claim 120, wherein the second recombinant adenovirus~~ (ii) comprises a nucleotide sequence encoding a polypeptide, or a fragment thereof, selected from acetylcholine, an androgen-receptor, an anti-PD-1 antibody heavy chain and/or light chain, an anti-PD-L1 antibody heavy chain and/or light chain, BORIS/CTCFL, BRAF, CD19, CD20, CD30, CD80, CD86, CD137, CD137L, CD154, CEA, DKK1/Wnt, EGFRvIII, FGF, gp100, Her-2/neu, ICAM, IL-1, IL-3, IL-4, IL-5, IL-6, IL-8, IL-9, IL-23A/p19, p40, IL-24, interferon-gamma, KRAS, MAGE, MAGE-A3, MART1, melan-A, mesothelin, MUC-1, NY-ESO-1, Podocalyxin (Podxl), p53, TGF-β, a TGF-β T~~t~~rap, thymidine kinase, and tyrosinase, or~~.~~

~~123. The method of claim 120, wherein the second recombinant adenovirus~~ (iii) comprises a nucleotide sequence encoding a cancer antigen derived from 9D7, androgen receptor, a BAGE family protein, β-catenin, BING-4, BRAF, BRCA1/2, a CAGE family protein, calcium-activated chloride channel 2, CD19, CD20, CD30, CDK4, CEA, CML66, CT9, CT10, cyclin-B1, EGFRvIII, Ep-CAM, EphA3, fibronectin, a GAGE family protein, gp100/pme1~~l~~17, Her-2/neu, HPV E6, HPV E7, Ig, immature laminin receptor, a MAGE family protein ~~(*e.g.*, MAGE-A3)~~, MART-1/melan-A, MART2, MC1R, mesothelin, a mucin family protein ~~(*e.g.*, MUC-1)~~, NY-ESO-1/LAGE-1, P.polypeptide, p53, podocalyxin (Podxl), PRAME, a ras family proteins ~~(*e.g.*, KRAS), p53, podocalyxin (podxl)~~, prostate specific antigen, a SAGE family protein, SAP-1, SSX-2, survivin, TAG-72, TCR, telomerase, TGF-βRII, TRP-1, TRP-2, tyrosinase, or a XAGE family protein.

~~124. The method of any one of claims 120-123, wherein the second recombinant adenovirus is an oncolytic adenovirus.~~

19~~125~~. Use of the pharmaceutical composition of claim 13 in the manufacture of a medicament for ~~A method of~~ lowering blood pressure in a subject ~~in need thereof, the method comprising administering to the subject an effective amount of the recombinant adenovirus of any one of claims 1-78 to lower blood pressure in the subject.~~

~~126. A method of~~ and/or increasing nitric oxide (NO) production in a subject ~~in need thereof, the method comprising administering to the subject an effective amount of the recombinant adenovirus of any one of claims 1-78 to increase nitric oxide (NO) production in the subject~~.

~~127. A method of treating and/or preventing hypertension in a subject in need thereof, the method comprising administering to the subject an effective amount of the recombinant adenovirus of any one of claims 1-78 to treat and/or prevent hypertension in the subject.~~

~~128. The method of any one of claims 82-127, wherein the subject is receiving or has received a VEGF inhibitor.~~

~~129. The method of any one of claims 80-128, wherein the effective amount of the recombinant adenovirus is 10^{2}-10^{15} plaque forming units (pfus).~~

~~130. The method of any one of claims 82-129, wherein the subject is a human or an animal.~~

~~131. The method of claim 130, wherein the subject is a pediatric human.~~

20. The pharmaceutical composition of claim 13 for use in therapy.