CLAIMS

1. An extracellular vesicle comprising an antisense oligonucleotide (ASO) which comprises a contiguous nucleotide sequence of 10 to 30 nucleotides in length that is complementary to a nucleic acid sequence within a *STAT6* transcript (SEQ ID NO: 1 or SEQ ID NO: 3), wherein the nucleic acid sequence within the *STAT6* transcript comprises a target region corresponding to:

a) nucleotides 2065-2084 of SEQ ID NO: 3;
b) nucleotides 1053-1067 of SEQ ID NO: 3;
c) nucleotides 1359-1373 of SEQ ID NO: 3;
d) nucleotides 1890-1904 of SEQ ID NO: 3;
e) nucleotides 1892-1906 of SEQ ID NO: 3;
f) nucleotides 1915-1929 of SEQ ID NO: 3;
g) nucleotides 1916-1930 of SEQ ID NO: 3;
h) nucleotides 1917-1931 of SEQ ID NO: 3;
i) nucleotides 1918-1932 of SEQ ID NO: 3;
j) nucleotides 1919-1933 of SEQ ID NO: 3;
k) nucleotides 1920-1934 of SEQ ID NO: 3;
l) nucleotides 1937-1951 of SEQ ID NO: 3;
m) nucleotides 1938-1952 of SEQ ID NO: 3;
n) nucleotides 2061-2075 of SEQ ID NO: 3;
o) nucleotides 2062-2076 of SEQ ID NO: 3;
p) nucleotides 2063-2077 of SEQ ID NO: 3;
q) nucleotides 2064-2078 of SEQ ID NO: 3;
r) nucleotides 2066-2080 of SEQ ID NO: 3;
s) nucleotides 2067-2081 of SEQ ID NO: 3;
t) nucleotides 2068-2082 of SEQ ID NO: 3;
u) nucleotides 2352-2366 of SEQ ID NO: 3;
v) nucleotides 3073-3087 of SEQ ID NO: 3;
w) nucleotides 1053-1068 of SEQ ID NO: 3;
x) nucleotides 1054-1069 of SEQ ID NO: 3;

y) nucleotides 1356-1371 of SEQ ID NO: 3;

z) nucleotides 1847-1862 of SEQ ID NO: 3;

aa) nucleotides 1886-1901 of SEQ ID NO: 3;

bb) nucleotides 1887-1902 of SEQ ID NO: 3;

cc) nucleotides 1888-1903 of SEQ ID NO: 3;

dd) nucleotides 1889-1904 of SEQ ID NO: 3;

ee) nucleotides 1890-1905 of SEQ ID NO: 3;

ff) nucleotides 1893-1908 of SEQ ID NO: 3;

gg) nucleotides 1917-1932 of SEQ ID NO: 3;

hh) nucleotides 1919-1934 of SEQ ID NO: 3;

ii) nucleotides 2056-2071 of SEQ ID NO: 3;

jj) nucleotides 2060-2075 of SEQ ID NO: 3;

kk) nucleotides 2066-2081 of SEQ ID NO: 3;

ll) nucleotides 2070-2085 of SEQ ID NO: 3;

mm) nucleotides 2351-2366 of SEQ ID NO: 3;

nn) nucleotides 2352-2367 of SEQ ID NO: 3;

oo) nucleotides 2359-2374 of SEQ ID NO: 3;

pp) nucleotides 3633-3648 of SEQ ID NO: 3;

qq) nucleotides 673-689 of SEQ ID NO: 3;

rr) nucleotides 1052-1068 of SEQ ID NO: 3;

ss) nucleotides 1356-1372 of SEQ ID NO: 3;

tt) nucleotides 1357-1373 of SEQ ID NO: 3;

uu) nucleotides 1359-1375 of SEQ ID NO: 3;

vv) nucleotides 1360-1376 of SEQ ID NO: 3;

ww) nucleotides 1839-1855 of SEQ ID NO: 3;

xx) nucleotides 1848-1864 of SEQ ID NO: 3;

yy) nucleotides 1849-1865 of SEQ ID NO: 3;

zz) nucleotides 1891-1907 of SEQ ID NO: 3;

aaa) nucleotides 1915-1931 of SEQ ID NO: 3;

bbb) nucleotides 1916-1932 of SEQ ID NO: 3;

ccc) nucleotides 1917-1933 of SEQ ID NO: 3;

ddd) nucleotides 1938-1954 of SEQ ID NO: 3;

eee) nucleotides 1939-1955 of SEQ ID NO: 3;

fff) nucleotides 2063-2079 of SEQ ID NO: 3;

ggg) nucleotides 2064-2080 of SEQ ID NO: 3;

hhh) nucleotides 2065-2081 of SEQ ID NO: 3;

iii) nucleotides 2066-2082 of SEQ ID NO: 3;

jjj) nucleotides 2068-2084 of SEQ ID NO: 3;

kkk) nucleotides 2187-2203 of SEQ ID NO: 3;

lll) nucleotides 2350-2366 of SEQ ID NO: 3;

mmm) nucleotides 2351-2367 of SEQ ID NO: 3;

nnn) nucleotides 2352-2368 of SEQ ID NO: 3;

ooo) nucleotides 2357-2373 of SEQ ID NO: 3;

ppp) nucleotides 513-532 of SEQ ID NO: 3;

qqq) nucleotides 671-690 of SEQ ID NO: 3;

rrr) nucleotides 1131-1150 of SEQ ID NO: 3;

sss) nucleotides 1354-1373 of SEQ ID NO: 3;

ttt) nucleotides 1355-1374 of SEQ ID NO: 3;

uuu) nucleotides 1356-1375 of SEQ ID NO: 3;

vvv) nucleotides 1432-1451 of SEQ ID NO: 3;

www) nucleotides 1555-1574 of SEQ ID NO: 3;

xxx) nucleotides 1556-1575 of SEQ ID NO: 3;

yyy) nucleotides 1557-1576 of SEQ ID NO: 3;

zzz) nucleotides 1558-1577 of SEQ ID NO: 3;

aaaa) nucleotides 1826-1845 of SEQ ID NO: 3;

bbbb) nucleotides 1827-1846 of SEQ ID NO: 3;

cccc) nucleotides 1833-1852 of SEQ ID NO: 3;

dddd) nucleotides 1843-1862 of SEQ ID NO: 3;

eeee) nucleotides 1846-1865 of SEQ ID NO: 3;

ffff) nucleotides 1847-1866 of SEQ ID NO: 3;

gggg) nucleotides 1883-1902 of SEQ ID NO: 3;

hhhh) nucleotides 1889-1908 of SEQ ID NO: 3;

iiii) nucleotides 1890-1909 of SEQ ID NO: 3;

jjjj) nucleotides 1891-1910 of SEQ ID NO: 3;

kkkk) nucleotides 1916-1935 of SEQ ID NO: 3;

llll) nucleotides 1917-1936 of SEQ ID NO: 3;

mmmm) nucleotides 2056-2075 of SEQ ID NO: 3;

nnnn) nucleotides 2057-2076 of SEQ ID NO: 3;

oooo) nucleotides 2060-2079 of SEQ ID NO: 3;

pppp) nucleotides 2062-2081 of SEQ ID NO: 3;

qqqq) nucleotides 2063-2082 of SEQ ID NO: 3;

rrrr) nucleotides 2068-2087 of SEQ ID NO: 3;

ssss) nucleotides 2347-2366 of SEQ ID NO: 3;

tttt) nucleotides 2348-2367 of SEQ ID NO: 3;

uuuu) nucleotides 2358-2377 of SEQ ID NO: 3;

vvvv) nucleotides 2782-2801 of SEQ ID NO: 3;

wwww) nucleotides 3070-3089 of SEQ ID NO: 3;

xxxx) nucleotides 3071-3090 of SEQ ID NO: 3; or

yyyy) nucleotides 3431-3450 of SEQ ID NO: 3.

2. The extracellular vesicle of claim 1, wherein the ASO comprises:

a) the nucleotide sequence set forth in SEQ ID NO: 185, with one or two mismatches; or

b) the nucleotide sequence set forth in a sequence selected from SEQ ID NOs: 91-184 and 186-193, with one or two mismatches.

3. The extracellular vesicle of claim 1, wherein the ASO comprises:

a) the nucleotide sequence set forth in SEQ ID NO: 185;

b) the nucleotide sequence set forth in a sequence selected from SEQ ID NO: 91-184 and 186-193.

4. The extracellular vesicle of any one of claims 1 to 3, wherein the ASO is a gapmer, a mixmer, or a totalmer.

5. The extracellular vesicle of any one of claims 1 to 4, wherein the ASO comprises one or more nucleoside analogs.

6. The extracellular vesicle of claim 5, wherein one or more of the nucleoside analogs comprises a 2'-O-alkyl-RNA; 2'-O-methyl RNA (2'-OMe); 2'-alkoxy-RNA; 2'-O-methoxyethyl-RNA (2'-MOE); 2'-amino-DNA; 2'-fluro-RNA; 2'-fluoro-DNA; arabino nucleic acid (ANA); 2'-fluoro-ANA; or bicyclic nucleoside analog.

7. The extracellular vesicle of claim 5 or 6, wherein one or more of the nucleoside analogs is a sugar modified nucleoside.

8. The extracellular vesicle of claim 7, wherein the sugar modified nucleoside is an affinity enhancing 2' sugar modified nucleoside.

9. The extracellular vesicle of any one of claims 5 to 8, wherein one or more of the nucleoside analogs comprises a nucleoside comprising a bicyclic sugar.

10. The extracellular vesicle of any one of claims 5 to 8, wherein one or more of the nucleoside analogs comprises an LNA.

11. The extracellular vesicle of any one of claims 5 to 10, wherein one or more of the nucleotide analogs is selected from the group consisting of constrained ethyl nucleoside (cEt), 2',4'-constrained 2′-O-methoxyethyl (cMOE), α-L-LNA, β-D-LNA, 2'-O,4'-C-ethylene-bridged nucleic acids (ENA), amino-LNA, oxy-LNA, thio-LNA, and any combination thereof.

12. The extracellular vesicle of any one of claims 1 to 11, wherein the ASO has the design of $LLLD_nLLL$, wherein "n" is 14, "L" is an LNA, and wherein "D" is a DNA.

13. The extracellular vesicle of any one of claims 1 to 12, wherein the ASO comprises one or more 5'-methyl-cytosine nucleobases.

14. The extracellular vesicle of claim 13, wherein all of the cytosine nucleobases in the ASO are 5'-methyl-cytosine nucleobases.

15. The extracellular vesicle of any one of claims 1 to 14, wherein the continuous nucleotide sequence is fully complementary to a nucleotide sequence within the STAT6 transcript.

16. The extracellular vesicle of any one of claims 1 to 15, wherein the ASO is from 14 to 20 nucleotides in length.

17. The extracellular vesicle of any one of claims 1 to 17, wherein the ASO is 20 nucleotides in length.

18. The extracellular vesicle of any one of claims 4 to 17, wherein the contiguous nucleotide sequence comprises one or more modified internucleoside linkages.

19. The extracellular vesicle of claim 18, wherein the one or more modified internucleoside linkages is a phosphorothioate linkage.

20. The extracellular vesicle of claim 18 or 19, wherein at least 75% of the internucleoside linkages are modified.

21. The extracellular vesicle of claim 20, wherein each of the internucleoside linkages in the ASO is a phosphorothioate linkage.

22. The extracellular vesicle of any one of claims 1 to 21, which further comprises an anchoring moiety.

23. The extracellular vesicle of claim 22, wherein the ASO is linked to the anchoring moiety.

24. The extracellular vesicle of any one of claims 1 to 23, further comprising an exogenous targeting moiety.

25. The extracellular vesicle of claim 24, wherein the EV comprises a scaffold moiety linking the exogenous targeting moiety to the EV.

26. The extracellular vesicle of claim 24 or 25, wherein the anchoring moiety and/or the scaffold moiety is a Scaffold X or a Scaffold Y.

27. The extracellular vesicle of claim 26, wherein the scaffold moiety is PTGFRN protein or a functional fragment thereof.

28. The extracellular vesicle of any one of claims 1 to 27, which overexpresses a PTGFRN protein or a functional fragment thereof.

29. The extracellular vesicle of claim 26, which comprises an amino acid sequence selected from the group consisting of (i) GGKLSKK (SEQ ID NO: 411), (ii) GAKLSKK (SEQ ID NO: 412), (iii) GGKQSKK (SEQ ID NO: 413), (iv) GGKLAKK (SEQ ID NO: 414), (v) GGKLSK (SEQ ID NO: 415), (vi) GGKLSKKK (SEQ ID NO: 438), (vii) GGKLSKKS (SEQ ID NO: 439), (viii) GAKLSKKK (SEQ ID NO: 440), (ix) GAKLSKKS (SEQ ID NO: 441), (x) GGKQSKKK (SEQ ID NO: 442), (xi) GGKQSKKS (SEQ ID NO: 443), (xii) GGKLAKKK (SEQ ID NO: 444), (xiii) GGKLAKKS (SEQ ID NO: 445), and (xiv) any combination thereof .

30. The extracellular vesicle of any one of claims 22 to 29, wherein the ASO is linked to the anchoring moiety on the exterior surface of the EV.

31. The extracellular vesicle of any one of claims 22 to 29, wherein the ASO is linked to the anchoring moiety on the luminal surface of the EV.

32. The extracellular vesicle of any one of claims 22 to 31, wherein the anchoring moiety comprises sterol, GM1, a lipid, a vitamin, a small molecule, a peptide, or a combination thereof.

33. The extracellular vesicle of any one of claims 22 to 32, wherein the anchoring moiety comprises cholesterol.

34. The extracellular vesicle of any one of claims 22 to 33, wherein the anchoring moiety comprises a phospholipid, a lysophospholipid, a fatty acid, a vitamin (e.g., vitamin D and/or vitamin E), or any combination thereof.

35. The extracellular vesicle of any one of claims 22 to 34, wherein the ASO is linked to the anchoring moiety by a linker.

36. The extracellular vesicle of claim 35, wherein the linker is a polypeptide, is a non-polypeptide moiety, or comprises ethylene glycol.

37. The extracellular vesicle of claim 35, wherein the linker comprises HEG, TEG, PEG, or any combination thereof.

38. The extracellular vesicle of any one of claims 35 to 37, wherein the linker is a cleavable linker.

39. The extracellular vesicle of any one of claims 1 to 38, wherein the EV is an exosome.

40. The extracellular vesicle of any one of claims 1 to 39, wherein the ASO is linked to cholesterol by a linker comprising TEG and HEG.

41. An extracellular vesicle comprising an antisense oligonucleotide (ASO) comprising the nucleotide sequence as set forth in SEQ ID NO: 185, wherein the ASO is 20 nucleotides in length and has the design of $LLLD_nLLL$, wherein "n" is 14, "L" is an LNA, and "D" is a DNA;

wherein all of the cytosine nucleobases in the ASO are 5'-methyl-cytosine nucleobases;

wherein each of the internucleoside linkages in the ASO is a phosphorothioate linkage;

wherein the ASO is linked to an anchoring moiety on the exterior surface of the extracellular vesicle;

wherein the anchoring moiety comprises cholesterol; and

wherein the ASO is linked to cholesterol by a linker comprising TEG and HEG.

42. The extracellular vesicle of claim 41, wherein the extracellular vesicle is an exosome.

43. An antisense oligonucleotide (ASO) comprising a contiguous nucleotide sequence of 10 to 30 nucleotides in length that is complementary to a nucleic acid sequence within a *STAT6* transcript (SEQ ID NO: 1 or SEQ ID NO: 3), wherein the nucleic acid sequence within the *STAT6* transcript comprises a target region corresponding to:

a) nucleotides 2065-2084 of SEQ ID NO: 3;

b) nucleotides 1053-1067 of SEQ ID NO: 3;

c) nucleotides 1359-1373 of SEQ ID NO: 3;

d) nucleotides 1890-1904 of SEQ ID NO: 3;

e) nucleotides 1892-1906 of SEQ ID NO: 3;

f) nucleotides 1915-1929 of SEQ ID NO: 3;

g) nucleotides 1916-1930 of SEQ ID NO: 3;

h) nucleotides 1917-1931 of SEQ ID NO: 3;

i) nucleotides 1918-1932 of SEQ ID NO: 3;

j) nucleotides 1919-1933 of SEQ ID NO: 3;

k) nucleotides 1920-1934 of SEQ ID NO: 3;

l) nucleotides 1937-1951 of SEQ ID NO: 3;

m) nucleotides 1938-1952 of SEQ ID NO: 3;

n) nucleotides 2061-2075 of SEQ ID NO: 3;

o) nucleotides 2062-2076 of SEQ ID NO: 3;

p) nucleotides 2063-2077 of SEQ ID NO: 3;

q) nucleotides 2064-2078 of SEQ ID NO: 3;

r) nucleotides 2066-2080 of SEQ ID NO: 3;

s) nucleotides 2067-2081 of SEQ ID NO: 3;

t) nucleotides 2068-2082 of SEQ ID NO: 3;

u) nucleotides 2352-2366 of SEQ ID NO: 3;

v) nucleotides 3073-3087 of SEQ ID NO: 3;

w) nucleotides 1053-1068 of SEQ ID NO: 3;

x) nucleotides 1054-1069 of SEQ ID NO: 3;

y) nucleotides 1356-1371 of SEQ ID NO: 3;

z) nucleotides 1847-1862 of SEQ ID NO: 3;

aa) nucleotides 1886-1901 of SEQ ID NO: 3;

bb) nucleotides 1887-1902 of SEQ ID NO: 3;

cc) nucleotides 1888-1903 of SEQ ID NO: 3;

dd) nucleotides 1889-1904 of SEQ ID NO: 3;

ee) nucleotides 1890-1905 of SEQ ID NO: 3;

ff) nucleotides 1893-1908 of SEQ ID NO: 3;

gg) nucleotides 1917-1932 of SEQ ID NO: 3;

hh) nucleotides 1919-1934 of SEQ ID NO: 3;

ii) nucleotides 2056-2071 of SEQ ID NO: 3;

jj) nucleotides 2060-2075 of SEQ ID NO: 3;

kk) nucleotides 2066-2081 of SEQ ID NO: 3;

ll) nucleotides 2070-2085 of SEQ ID NO: 3;

mm) nucleotides 2351-2366 of SEQ ID NO: 3;

nn) nucleotides 2352-2367 of SEQ ID NO: 3;

oo) nucleotides 2359-2374 of SEQ ID NO: 3;

pp) nucleotides 3633-3648 of SEQ ID NO: 3;

qq) nucleotides 673-689 of SEQ ID NO: 3;

rr) nucleotides 1052-1068 of SEQ ID NO: 3;

ss) nucleotides 1356-1372 of SEQ ID NO: 3;

tt) nucleotides 1357-1373 of SEQ ID NO: 3;

uu) nucleotides 1359-1375 of SEQ ID NO: 3;

vv) nucleotides 1360-1376 of SEQ ID NO: 3;

ww) nucleotides 1839-1855 of SEQ ID NO: 3;

xx) nucleotides 1848-1864 of SEQ ID NO: 3;

yy) nucleotides 1849-1865 of SEQ ID NO: 3;

zz) nucleotides 1891-1907 of SEQ ID NO: 3;

aaa) nucleotides 1915-1931 of SEQ ID NO: 3;

bbb) nucleotides 1916-1932 of SEQ ID NO: 3;

ccc) nucleotides 1917-1933 of SEQ ID NO: 3;

ddd) nucleotides 1938-1954 of SEQ ID NO: 3;

eee) nucleotides 1939-1955 of SEQ ID NO: 3;

fff) nucleotides 2063-2079 of SEQ ID NO: 3;

ggg) nucleotides 2064-2080 of SEQ ID NO: 3;

hhh) nucleotides 2065-2081 of SEQ ID NO: 3;

iii) nucleotides 2066-2082 of SEQ ID NO: 3;

jjj) nucleotides 2068-2084 of SEQ ID NO: 3;

kkk) nucleotides 2187-2203 of SEQ ID NO: 3;

lll) nucleotides 2350-2366 of SEQ ID NO: 3;

mmm) nucleotides 2351-2367 of SEQ ID NO: 3;

nnn) nucleotides 2352-2368 of SEQ ID NO: 3;

ooo) nucleotides 2357-2373 of SEQ ID NO: 3;

ppp) nucleotides 513-532 of SEQ ID NO: 3;

qqq) nucleotides 671-690 of SEQ ID NO: 3 ;

rrr) nucleotides 1131-1150 of SEQ ID NO: 3;

sss) nucleotides 1354-1373 of SEQ ID NO: 3;

ttt) nucleotides 1355-1374 of SEQ ID NO: 3;

uuu) nucleotides 1356-1375 of SEQ ID NO: 3;

vvv) nucleotides 1432-1451 of SEQ ID NO: 3;

www) nucleotides 1555-1574 of SEQ ID NO: 3;

xxx) nucleotides 1556-1575 of SEQ ID NO: 3;

yyy) nucleotides 1557-1576 of SEQ ID NO: 3;

zzz) nucleotides 1558-1577 of SEQ ID NO: 3;

aaaa) nucleotides 1826-1845 of SEQ ID NO: 3;

bbbb) nucleotides 1827-1846 of SEQ ID NO: 3;

cccc) nucleotides 1833-1852 of SEQ ID NO: 3;

dddd) nucleotides 1843-1862 of SEQ ID NO: 3;

eeee) nucleotides 1846-1865 of SEQ ID NO: 3;

ffff) nucleotides 1847-1866 of SEQ ID NO: 3;

gggg) nucleotides 1883-1902 of SEQ ID NO: 3;

hhhh) nucleotides 1889-1908 of SEQ ID NO: 3;

iiii) nucleotides 1890-1909 of SEQ ID NO: 3;

jjjj) nucleotides 1891-1910 of SEQ ID NO: 3;

kkkk) nucleotides 1916-1935 of SEQ ID NO: 3;

llll) nucleotides 1917-1936 of SEQ ID NO: 3;

mmmm) nucleotides 2056-2075 of SEQ ID NO: 3;

nnnn) nucleotides 2057-2076 of SEQ ID NO: 3;

oooo) nucleotides 2060-2079 of SEQ ID NO: 3;

pppp) nucleotides 2062-2081 of SEQ ID NO: 3;

qqqq) nucleotides 2063-2082 of SEQ ID NO: 3;

rrrr) nucleotides 2068-2087 of SEQ ID NO: 3;

ssss) nucleotides 2347-2366 of SEQ ID NO: 3;

tttt) nucleotides 2348-2367 of SEQ ID NO: 3;

uuuu) nucleotides 2358-2377 of SEQ ID NO: 3;

vvvv) nucleotides 2782-2801 of SEQ ID NO: 3;

wwww) nucleotides 3070-3089 of SEQ ID NO: 3;

xxxx) nucleotides 3071-3090 of SEQ ID NO: 3; or

yyyy) nucleotides 3431-3450 of SEQ ID NO: 3.

44. A conjugate comprising the ASO of claim 43, wherein the ASO is covalently attached to at least one non-nucleotide or non-polynucleotide moiety.

45. An extracellular vesicle comprising the ASO of claim 43 or the conjugate of claim 44.

46. A pharmaceutical composition comprising the extracellular vesicle of any one of claims 1 to 42 and 45, the ASO of claim 43, or the conjugate of claim 44, and a pharmaceutically acceptable diluent, carrier, salt, or adjuvant.

47. A kit comprising the extracellular vesicle of any one of claims 1 to 42 and 45, the ASO of claim 43, the conjugate of claim 44, or the pharmaceutical composition of claim 46, and instructions for use.

48. A diagnostic kit comprising the extracellular vesicle of any one of claims 1 to 42 and 45, the ASO of claim 43, the conjugate of claim 44, or the pharmaceutical composition of claim 46, and instructions for use.

49. Use of the extracellular vesicle of any one of claims 1 to 42 and 45, the ASO of claim 43, the conjugate of claim 44, or the pharmaceutical composition of claim 46 in the manufacture of a medicament for the treatment of a cancer in a subject in need thereof.

50. Use of the extracellular vesicle of any one of claims 1 to 42 and 45, the ASO of claim 43, the conjugate of claim 44, or the pharmaceutical composition of claim 46 in the manufacture of a medicament for the treatment of a disease or disorder in a subject in need thereof, wherein the disease or disorder is selected from a fibrosis, an inflammation, a neurodegenerative disease, a metabolic disorder/CVD, and any combination thereof.