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.

~~2. The extracellular vesicle of claim 1, wherein the ASO is not TGAGCGAATGGACAGGTCTT (SEQ ID NO: 89).~~

3. The extracellular vesicle of claim 1 or 2, which targets a cell selected from the group consisting of a macrophage, a myeloid-derived suppressor cell (MDSC), a monocyte, a basophil, a neutrophil, an eosinophil, and any combination thereof.

4. The extracellular vesicle of any one of claims 1 to 3, wherein the ASO comprises a contiguous nucleotide sequence of 10 to 30 nucleotides in length that is complementary to a nucleic acid sequence within nucleotides 1 to 2056 of a STAT6 transcript corresponding to a nucleotide sequence as set forth in SEQ ID NO: 3 or nucleotides 2059 to 3963 of a STAT6 transcript corresponding to a nucleotide sequence as set forth in SEQ ID NO: 3.

5. The extracellular vesicle of claim 4, wherein the contiguous nucleotide sequence is at least about 80%, at least about 85%, at least about 90%, at least about 95%, or about 100% complementary to the nucleic acid sequence within the STAT6 transcript.

6. The extracellular vesicle of any one of claims 1 to 5, wherein the ASO is capable of reducing STAT6 protein expression in a human cell (e.g., an immune cell), wherein the human cell expresses the STAT6 protein.

7. The extracellular vesicle of claim 6, wherein the STAT6 protein expression is reduced by at least about 30%, at least about 35%, at least about 40%, at least about 45%, at least about 50%, at least about 55%, at least about 60%, at least about 65%, at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, or about 100% compared to STAT6 protein expression in a human cell that is not exposed to the ASO.

8. The extracellular vesicle of any one of claims 1 to 7, wherein the ASO is capable of reducing a level of STAT6 mRNA in a human cell (e.g., an immune cell), wherein the human cell expresses the STAT6 mRNA.

9. The extracellular vesicle of claim 8, wherein the level of STAT6 mRNA is reduced by at least about 30%, at least about 35%, at least about 40%, at least about 45%, at least about 50%, at least about 55%, at least about 60%, at least about 65%, at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, or about 100% compared to the level of the STAT6 mRNA in a human cell that is not exposed to the ASO.

~~10~~4. The extracellular vesicle of any one of claims 1 to ~~9~~3, wherein the ASO is a gapmer, a mixmer, or a totalmer.

~~11~~5. The extracellular vesicle of any one of claims 1 to ~~10~~4, wherein the ASO comprises one or more nucleoside analogs.

~~12~~6. The extracellular vesicle of claim ~~11~~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.

~~13~~7. The extracellular vesicle of claim ~~11~~ 5 or ~~12~~6, wherein one or more of the nucleoside analogs is a sugar modified nucleoside.

~~14~~8. The extracellular vesicle of claim ~~13~~7, wherein the sugar modified nucleoside is an affinity enhancing 2' sugar modified nucleoside.

~~15~~9. The extracellular vesicle of any one of claims ~~11~~ 5 to ~~14~~8, wherein one or more of the nucleoside analogs comprises a nucleoside comprising a bicyclic sugar.

~~16~~10. The extracellular vesicle of any one of claims ~~11~~ 5 to ~~14~~8, wherein one or more of the nucleoside analogs comprises an LNA.

~~17~~11. The extracellular vesicle of any one of claims ~~11~~ 5 to ~~16~~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.

~~18~~13. The extracellular vesicle of any one of claims 1 to 12~~17~~, 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.

~~19. The extracellular vesicle of any one of claims 4 to 18, wherein the contiguous nucleotide sequence is complementary to a nucleic acid sequence within (i) a 5' untranslated region (UTR); (ii) a coding region; or (iii) a 3' UTR of the STAT6 transcript.~~

~~20. The extracellular vesicle of any one of claims 1 to 19, wherein the contiguous nucleotide sequence is complementary to a nucleic acid sequence comprising (i) nucleotides 1 – 700 of SEQ ID NO: 3; (ii) nucleotides 1000-1500 of SEQ ID NO: 3; (iii) nucleotides 1500 - 2000 of SEQ ID NO: 3; (iv) nucleotides 2000 – 2500 of SEQ ID NO: 3; (v) 2500 – 3000 of SEQ ID NO: 3; (vi) 3000 – 3700 of SEQ ID NO: 3, (vii) nucleotides 413 – 803 of SEQ ID NO: 3; (viii) nucleotides 952-1688 of SEQ ID NO: 3; (ix) nucleotides 1726 - 2489 of SEQ ID NO: 3; (x) nucleotides 2682 – 2912 of SEQ ID NO: 3; (xi) 2970 – 3203 of SEQ ID NO: 3; (xii) 3331 – 3561 of SEQ ID NO: 3; (xiii) nucleotides 463 – 753 of SEQ ID NO: 3; (xiv) nucleotides 1002-1638 of SEQ ID NO: 3; (xv) nucleotides 1776 - 2439 of SEQ ID NO: 3; (xvi) nucleotides 2682 – 2862 of SEQ ID NO: 3; (xvii) 3020 – 3153 of SEQ ID NO: 3; (xviii) 3381 – 3511 of SEQ ID NO: 3; (xix) nucleotides 503 – 713 of SEQ ID NO: 3; (xx) nucleotides 1042-1598 of SEQ ID NO: 3; (xxi) nucleotides 1816 - 2399 of SEQ ID NO: 3; (xxii) nucleotides 2722 – 2822 of SEQ ID NO: 3; (xxiii) 3060 – 3113 of SEQ ID NO: 3; or (xxiv) 3421 – 3471 of SEQ ID NO: 3.~~

~~21. The extracellular vesicle of any one of claims 1 to 20, wherein the contiguous nucleotide sequence is complementary to a nucleic acid sequence within (i) (i) nucleotides 513 – 703 of SEQ ID NO: 3; (ii) nucleotides 1052 – 1588 of SEQ ID NO: 3; (iii) nucleotides 1826 – 2389 of SEQ ID NO: 3; (iv) nucleotides 2732 – 2812 of SEQ ID NO: 3; (v) 3070 – 3103 of SEQ ID NO: 3; or (vi) 3431 – 3461 of SEQ ID NO: 3.~~

~~22. The extracellular vesicle of any one of claims 1 to 21, wherein the contiguous nucleotide sequence comprises a nucleotide sequence complementary to a sequence selected from the sequences in FIG. 1.~~

~~23~~15. The extracellular vesicle of any one of claims ~~14~~ 1 to ~~22~~14, wherein the continuous nucleotide sequence is fully complementary to a nucleotide sequence within the STAT6 transcript.

~~24. The extracellular vesicle of any one of claims 13 to 31, wherein the ASO comprises a nucleotide sequence selected from SEQ ID NOs: 91-193, with one or two mismatches.~~

~~25. The extracellular vesicle of any one of claims 1 to 24, wherein the ASO has a design selected from the group consisting of the designs in FIG. 1, wherein the upper letter is a sugar modified nucleoside and the lower case letter is DNA.~~

~~26~~16. The extracellular vesicle of any one of claims 1 to ~~25~~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.

~~27~~18. The extracellular vesicle of any one of claims 4 to ~~26~~17, wherein the contiguous nucleotide sequence comprises one or more modified internucleoside linkages.

~~28~~19. The extracellular vesicle of claim ~~35~~18, wherein the one or more modified internucleoside linkages is a phosphorothioate linkage.

~~29~~20. The extracellular vesicle of claim ~~27~~ 18 or 19~~28~~, wherein at least 75%~~, at least 80%, at least 85%, at least 90%, at least 95%, or 100%~~ of the internucleoside linkages are modified.

~~30~~21. The extracellular vesicle of claim 20~~29~~, wherein each of the internucleoside linkages in the ASO is a phosphorothioate linkage.

~~31~~22. The extracellular vesicle of any one of claims 1 to 21~~30~~, which further comprises an anchoring moiety.

~~32~~23. The extracellular vesicle of claim 22~~31~~, wherein the ASO is linked to the anchoring moiety.

~~33~~24. The extracellular vesicle of any one of claims 1 to 23~~32~~, further comprising an exogenous targeting moiety.

~~34. The extracellular vesicle of claim 33, wherein the exogenous targeting moiety comprises a peptide, an antibody or an antigen binding fragment thereof, a chemical compound, an RNA aptamer, or any combination thereof.~~

~~35. The extracellular vesicle of claim 33 or 34, wherein the exogenous targeting moiety comprises a peptide.~~

~~36. The extracellular vesicle of any one of claims 33 to 35, wherein the exogenous targeting moiety comprises a microprotein, a designed ankyrin repeat protein (darpin), an anticalin, an adnectin, an aptamer, a peptide mimetic molecule, a natural ligand for a receptor, a camelid nanobody, or any combination thereof.~~

~~37. The extracellular vesicle of any one of claims 33 to 36, wherein the exogenous targeting moiety comprises a full-length antibody, a single domain antibody, a heavy chain only antibody (VHH), a single chain antibody, a shark heavy chain only antibody (VNAR), an scFv, a Fv, a Fab, a Fab', a F(ab')2, or any combination thereof.~~

~~38. The extracellular vesicle of claim 37, wherein the antibody is a single chain antibody.~~

~~39. The extracellular vesicle of any one of claims 33 to 38, wherein the exogenous targeting moiety targets the exosome to the liver, heart, lungs, brain, kidneys, central nervous system, peripheral nervous system, muscle, bone, joint, skin, intestine, bladder, pancreas, lymph nodes, spleen, blood, bone marrow, or any combination thereof.~~

~~40. The extracellular vesicle of any one of claims 33 to 39, wherein the exogenous targeting moiety targets the exosome to a tumor cell, dendritic cell, T cell, B cell, macrophage, neuron, hepatocyte, Kupffer cell, myeloid-lineage cell (e.g., a neutrophils, monocytes, macrophages, hematopoietic stem cell, an MDSC (e.g., a monocytic MDSC or a granulocytic MDSC)), or any combination thereof.~~

~~41~~25. The extracellular vesicle of ~~any one of claims 33 to 40~~claim 24, wherein the EV comprises a scaffold moiety linking the exogenous targeting moiety to the EV.

~~42~~26. The extracellular vesicle of ~~any one of claims 33 to 41~~claim 24 or 25, wherein the anchoring moiety and/or the scaffold moiety is a Scaffold X or a Scaffold Y.

~~43. The extracellular vesicle of any one of claims 33 to 41, wherein the anchoring moiety and/or the scaffold moiety is a Scaffold Y.~~

~~44. The extracellular vesicle of claim 42, wherein the Scaffold X is a scaffold protein that is capable of anchoring the ASO on the luminal surface of the EV and/or on the exterior surface of the EV.~~

~~45. The extracellular vesicle of claim 42 or 44, wherein the Scaffold X is selected from the group consisting of prostaglandin F2 receptor negative regulator (the PTGFRN protein); basigin (the BSG protein); immunoglobulin superfamily member 2 (the IGSF2 protein); immunoglobulin superfamily member 3 (the IGSF3 protein); immunoglobulin superfamily member 8 (the IGSF8 protein); integrin beta-1 (the ITGB1 protein); integrin alpha-4 (the ITGA4 protein); 4F2 cell-surface antigen heavy chain (the SLC3A2 protein); a class of ATP transporter proteins (the ATP1A1, ATP1A2, ATP1A3, ATP1A4, ATP1B3, ATP2B1, ATP2B2, ATP2B3, ATP2B4 proteins); a functional fragment thereof; and any combination thereof.~~

~~46~~27. The extracellular vesicle of ~~any one of claims 31 to 45~~claim 26, wherein ~~the anchoring moiety and/or~~ the scaffold moiety is PTGFRN protein or a functional fragment thereof.

~~47. The extracellular vesicle of any one of claims 31 to 46, wherein the anchoring moiety and/or the scaffold moiety comprises an amino acid sequence as set forth in SEQ ID NO: 302.~~

~~48. The extracellular vesicle of any one of claims 31 to 47, wherein the anchoring moiety and/or the scaffold moiety comprises an amino acid sequence at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or about 100% identical to SEQ ID NO: 301.~~

~~42~~28. The extracellular vesicle of any one of claims 1 to 27, which overexpresses a PTGFRN protein or a functional fragment thereof.

~~49. The extracellular vesicle of claim 43, wherein the Scaffold Y is a scaffold protein that is capable of anchoring the ASO on the luminal surface of the EV and/or on the exterior surface of the EV.~~

~~50. The extracellular vesicle of claim 43 or 49, wherein the Scaffold Y is selected from the group consisting of myristoylated alanine rich Protein Kinase C substrate (the MARCKS protein),~~

~~myristoylated alanine rich Protein Kinase C substrate like 1 (the MARCKSL1 protein), brain acid soluble protein 1 (the BASP1 protein), a functional fragment thereof, and any combination thereof.~~

~~51. The extracellular vesicle of any one of claims 43, 49, and 50, wherein the Scaffold Y is a BASP1 protein or a functional fragment thereof.~~

~~52. The extracellular vesicle of any one of claims 43 and 49 to 51, wherein the Scaffold Y comprises an N terminus domain (ND) and an effector domain (ED), wherein the ND and/or the ED are associated with the luminal surface of the EV.~~

~~53. The extracellular vesicle of claim 52, wherein the ND is associated with the luminal surface of the exosome via myristoylation.~~

~~54. The extracellular vesicle of claim 52 or 53, wherein the ED is associated with the luminal surface of the exosome by an ionic interaction.~~

~~55. The extracellular vesicle of any one of claims 52 to 53, wherein the ED comprises (i) a basic amino acid or (ii) two or more basic amino acids in sequence, wherein the basic amino acid is selected from the group consisting of Lys, Arg, His, and any combination thereof.~~

~~56. The extracellular vesicle of claim 55, wherein the basic amino acid is (Lys)n, wherein n is an integer between 1 and 10.~~

~~57. The extracellular vesicle of any one of claims 52 to 56, wherein the ED comprises Lys (K), KK, KKK, KKKK (SEQ ID NO: 405), KKKKK (SEQ ID NO: 406), Arg (R), RR, RRR, RRRR (SEQ ID NO: 407); RRRRR (SEQ ID NO: 408), KR, RK, KKR, KRK, RKK, KRR, RRK, (K/R)(K/R)(K/R)(K/R) (SEQ ID NO: 409), (K/R)(K/R)(K/R)(K/R)(K/R) (SEQ ID NO: 410), or any combination thereof.~~

~~58. The extracellular vesicle of any one of claims 52 to 57, wherein the ND comprises the amino acid sequence as set forth in G:X2:X3:X4:X5:X6, wherein G represents Gly; wherein ":" represents a peptide bond, wherein each of the X2 to the X6 is independently an amino acid, and wherein the X6 comprises a basic amino acid.~~

~~59. The extracellular vesicle of claim 58, wherein:~~

(i) the X2 is selected from the group consisting of Pro, Gly, Ala, and Ser;

(ii) the X4 is selected from the group consisting of Pro, Gly, Ala, Ser, Val, Ile, Leu, Phe, Trp, Tyr, Gln and Met;

(iii) the X5 is selected from the group consisting of Pro, Gly, Ala, and Ser;

(iv) the X6 is selected from the group consisting of Lys, Arg, and His; or

(v) any combination of (i)-(iv).

60. The extracellular vesicle of any one of claims 52 to 59, wherein the ND comprises the amino acid sequence of G:X2:X3:X4:X5:X6, wherein

(i) G represents Gly;

(ii) ":" represents a peptide bond;

(iii) the X2 is an amino acid selected from the group consisting of Pro, Gly, Ala, and Ser;

(iv) the X3 is an amino acid;

(v) the X4 is an amino acid selected from the group consisting of Pro, Gly, Ala, Ser, Val, Ile, Leu, Phe, Trp, Tyr, Gln and Met;

(vi) the X5 is an amino acid selected from the group consisting of Pro, Gly, Ala, and Ser; and

(vii) the X6 is an amino acid selected from the group consisting of Lys, Arg, and His.

61. The extracellular vesicle of any one of claims 58 to 60, wherein the X3 is selected from the group consisting of Asn, Gln, Ser, Thr, Asp, Glu, Lys, His, and Arg.

62. The extracellular vesicle of any one of claims 52 to 61, wherein the ND and the ED are joined by a linker.

63. The extracellular vesicle of claim 62, wherein the linker comprises one or more amino acids.

~~64~~29. The extracellular vesicle~~method~~ of ~~any one of claims 52 to 63~~claim 26, ~~wherein the ND~~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 ~~or (vi) any combination thereof~~.

~~65. The extracellular vesicle of claim 64, wherein the ND comprises an amino acid sequence selected from the group consisting of (i) GGKLSKKK (SEQ ID NO: 438), (ii) GGKLSKKS (SEQ ID NO: 439), (iii) GAKLSKKK (SEQ ID NO: 440), (iv) GAKLSKKS (SEQ ID NO: 441), (v) GGKQSKKK (SEQ ID NO: 442), (vi) GGKQSKKS (SEQ ID NO: 443), (vii) GGKLAKKK (SEQ ID NO: 444), (viii) GGKLAKKS (SEQ ID NO: 445), and (ix) any combination thereof.~~

~~66. The extracellular vesicle of any one of claims 52 to 65, wherein the ND comprises the amino acid sequence GGKLSKK (SEQ ID NO: 411).~~

~~67. The extracellular vesicle of any one of claims 43 and 49 to 66, wherein the Scaffold Y is at least about 8, at least about 9, at least about 10, at least about 11, at least about 12, at least about 13, at least about 14, at least about 15, at least about 16, at least about 17, at least about 18, at least about 19, at least about 20, at least about 21, at least about 22, at least about 23, at least about 24, at least about 25, at least about 30, at least about 35, at least about 40, at least about 45, at least about 50, at least about 55, at least about 60, at least about 65, at least about 70, at least about 75, at least about 80, at least about 85, at least about 90, at least about 95, at least about 100, at least about 105, at least about 110, at least about 120, at least about 130, at least about 140, at least about 150, at least about 160, at least about 170, at least about 180, at least about 190, or at least about 200 amino acids in length.~~

~~68. The extracellular vesicle of claims 43 and 49 to 67, wherein the Scaffold Y comprises (i) GGKLSKKKKGYNVN (SEQ ID NO: 446), (ii) GAKLSKKKKGYNVN (SEQ ID NO: 447), (iii) GGKQSKKKKGYNVN (SEQ ID NO: 448), (iv) GGKLAKKKKGYNVN (SEQ ID NO: 449), (v) GGKLSKKKKGYSGG (SEQ ID NO: 450), (vi) GGKLSKKKKGSGGS (SEQ ID NO: 451), (vii)~~

~~GGKLSKKKKSGGSG (SEQ ID NO: 452), (viii) GGKLSKKKSGGSGG (SEQ ID NO: 453), (ix) GGKLSKKSGGSGGS (SEQ ID NO: 454), (x) GGKLSKSGGSGGSV (SEQ ID NO: 455), or (xi) GAKKSKKRFSFKKS (SEQ ID NO: 456).~~

~~69. The extracellular vesicle of claims 43 and 49 to 68, wherein the Scaffold Y consists of (i) GGKLSKKKKGYNVN (SEQ ID NO: 446), (ii) GAKLSKKKKGYNVN (SEQ ID NO: 447), (iii) GGKQSKKKKGYNVN (SEQ ID NO: 448), (iv) GGKLAKKKKGYNVN (SEQ ID NO: 449), (v) GGKLSKKKKGYSGG (SEQ ID NO: 450), (vi) GGKLSKKKKGSGGS (SEQ ID NO: 451), (vii) GGKLSKKKKSGGSG (SEQ ID NO: 452), (viii) GGKLSKKKSGGSGG (SEQ ID NO: 453), (ix) GGKLSKKSGGSGGS (SEQ ID NO: 454), (x) GGKLSKSGGSGGSV (SEQ ID NO: 455), or (xi) GAKKSKKRFSFKKS (SEQ ID NO: 456).~~

~~70. The extracellular vesicle of claim 43 and 49 to 69, wherein the Scaffold Y does not comprise Met at the N terminus.~~

~~71. The extracellular vesicle of any one of claims 43 and 49 to 70, wherein the Scaffold Y comprises a myristoylated amino acid residue at the N terminus of the scaffold protein.~~

~~72. The extracellular vesicle of claim 71, wherein the amino acid residue at the N terminus of the Scaffold Y is Gly.~~

~~73~~30. The extracellular vesicle of any one of claims ~~31~~ 22 to ~~72~~29, wherein the ASO is linked to the anchoring moiety ~~and/or the scaffold moiety~~ on the exterior surface of the EV.

~~74~~31. The extracellular vesicle of any one of claims ~~31~~ 22 to ~~73~~29, wherein the ASO is linked to the anchoring moiety ~~and/or the scaffold moiety~~ on the luminal surface of the EV.

~~75~~32. The extracellular vesicle of any one of claims ~~31~~ 22 to ~~74~~31, wherein the anchoring moiety comprises sterol, GM1, a lipid, a vitamin, a small molecule, a peptide, or a combination thereof.

~~76~~33. The extracellular vesicle of any one of claims ~~31~~ 22 to ~~74~~32, wherein the anchoring moiety comprises cholesterol.

~~77~~34. The extracellular vesicle of any one of claims ~~31~~ 22 to ~~74~~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.

~~78~~35. The extracellular vesicle of any one of claims ~~31~~ 22 to ~~77~~34, wherein the ASO is linked to the anchoring moiety ~~and/or the scaffold moiety~~ by a linker.

~~79. The extracellular vesicle of any one of claims 1 to 78, wherein the ASO is linked to the EV by a linker.~~

~~80~~36. The extracellular vesicle of claim ~~78 or 79~~35, wherein the linker is a polypeptide, is a non-polypeptide moiety, or comprises ethylene glycol.

~~81. The extracellular vesicle of claim 78 or 79, wherein the linker is a non-polypeptide moiety.~~

~~82. The extracellular vesicle of claim 78 or 79, wherein the linker comprise ethylene glycol.~~

~~83~~37. The extracellular vesicle of claim 35~~82~~, wherein the linker comprises HEG, TEG, PEG, or any combination thereof.

~~84. The extracellular vesicle of claim 78 or 79, wherein the linker comprises acrylic phosphoramidite (e.g,. ACRYDITE™), adenylation, azide (NHS Ester), digoxigenin (NHS Ester), cholesterol-TEG, I-LINKER™, an amino modifier (e.g., amino modifier C6, amino modifier C12, amino modifier C6 dT, or Uni-Link™ amino modifier), alkyne, 5' Hexynyl, 5-Octadiynyl dU, biotinylation (e.g., biotin, biotin (Azide), biotin dT, biotin-TEG, dual biotin, PC biotin, or desthiobiotin), thiol modification (thiol modifier C3 S-S, dithiol or thiol modifier C6 S-S), or any combination thereof.~~

~~85~~38. The extracellular vesicle of any one of claims ~~78 to 84~~35 to 37, wherein the linker is a cleavable linker.

~~86. The extracellular vesicle of claim 85, wherein the linker comprises valine-alanine-p-aminobenzylcarbamate or valine-citrulline-p-aminobenzylcarbamate.~~

~~87. The extracellular vesicle of any one of claims 78 to 86, wherein the linker comprises (i) a maleimide moiety and (ii) valine-alanine-p-aminobenzylcarbamate or valine-citrulline-p-aminobenzylcarbamate.~~

~~88~~39. The extracellular vesicle of any one of claims 1 to ~~87~~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.

~~89~~43. An antisense oligonucleotide (ASO) comprising ~~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

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

~~90. The ASO of claim 89, which is not TGAGCGAATGGACAGGTCTT (SEQ ID NO: 89).~~

~~91. The ASO of claim 89 or 90, which comprises a contiguous nucleotide sequence of 10 to 30 nucleotides in length that is complementary to a nucleic acid sequence within nucleotides 1 to 2056 of a STAT6 transcript corresponding to a nucleotide sequence as set forth in SEQ ID NO: 3, nucleotides 2059 to 3963 of a STAT6 transcript corresponding to a nucleotide sequence as set forth in SEQ ID NO: 3.~~

~~92. The ASO of claim 91, wherein the contiguous nucleotide sequence thereof is at least about 80%, at least about 85%, at least about 90%, at least about 95%, or about 100% complementary to the nucleic acid sequence within the STAT6 transcript.~~

~~93. The ASO of any one of claims 89 to 92, which is capable of reducing STAT6 protein expression in a human cell (e.g., an immune cell), wherein the human cell expresses the STAT6 protein.~~

~~94. The ASO of claim 93, wherein the STAT6 protein expression is reduced by at least about 30%, at least about 35%, at least about 40%, at least about 45%, at least about 50%, at least about 55%, at least about 60%, at least about 65%, at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, or about 100% compared to STAT6 protein expression in a human cell that is not exposed to the ASO.~~

~~95. The ASO of any one of claims 89 to 94, which is capable of reducing a level of STAT6 mRNA in a human cell (e.g., an immune cell), wherein the human cell expresses the STAT6 mRNA.~~

~~96. The ASO of claim 95, wherein the level of STAT6 mRNA is reduced by at least about 30%, at least about 35%, at least about 40%, at least about 45%, at least about 50%, at least about 55%, at least about 60%, at least about 65%, at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, or about 100% compared to the level of the STAT6 mRNAin a human cell that is not exposed to the ASO.~~

~~97. The ASO of any one of claims 91 to 96, which is a gapmer, a mixmer, or a totalmer.~~

~~98. The ASO of any one of claims 91 to 97, which comprises one or more nucleoside analogs.~~

~~99. The ASO of claim 98, 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 (LNA).~~

~~100. The ASO of claim 98 or 99, wherein one or more of the nucleoside analogs is a sugar modified nucleoside.~~

~~101. The ASO of claim 100, wherein the sugar modified nucleoside is an affinity enhancing 2' sugar modified nucleoside.~~

~~102. The ASO of any one of claims 97 to 101, wherein one or more of the nucleoside analogs comprises a nucleoside comprising a bicyclic sugar.~~

~~103. The ASO of any one of claims 97 to 102, wherein one or more of the nucleoside analogs comprises an LNA.~~

~~104. The ASO of claim 103, wherein the LNA 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.~~

~~105. The ASO of any one of claims 89 to 104, which comprises one or more 5'-methyl-cytosine nucleobases.~~

~~106. The ASO of any one of claims 89 to 105, wherein the ASO comprises any one of SEQ ID NO: 194 to SEQ ID NO: 206.~~

~~107. The ASO of any one of claims 89 to 106, wherein the ASO has a design selected from the group consisting of the designs in FIG. 1, wherein the upper letter is a sugar modified nucleoside and the lower case letter is DNA.~~

~~108. The ASO of any one of claims 89 to 107, wherein the ASO is from 14 to 20 nucleotides in length.~~

~~109. The ASO of any one of claims 89 to 108, wherein the contiguous nucleotide sequence comprises one or more modified internucleoside linkages.~~

~~110. The ASO of claim 109, wherein the one or more modified internucleoside linkages is a phosphorothioate linkage.~~

~~111. The ASO of claim 109 or 110, wherein at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or 100% of internucleoside linkages are modified.~~

~~112. The ASO of claim 111, wherein each of the internucleoside linkages in the ASO is a phosphorothioate linkage.~~

~~113~~44. A conjugate comprising the ASO of claim 43 ~~any one of claims 89 to 112~~, wherein the ASO is covalently attached to at least one non-nucleotide or non-polynucleotide moiety.

~~114. The conjugate of claim 113, wherein the non-nucleotide or non-polynucleotide moiety comprises a protein, a fatty acid chain, a sugar residue, a glycoprotein, a polymer, or any combinations thereof.~~

~~115~~45. An extracellular vesicle comprising the ASO of ~~any one of claims 89 to 112~~claim 43 or the conjugate of claim 44~~113 or 114~~.

~~116~~46. A pharmaceutical composition comprising the extracellular vesicle of any one of claims 1 to ~~88~~ 42 and ~~115~~45, the ASO of ~~any one of claims 89 to 112~~claim 43, or the conjugate of claim 44~~113 or 114~~, and a pharmaceutically acceptable diluent, carrier, salt, or adjuvant.

~~117. The pharmaceutical composition of claim 116, wherein the pharmaceutically acceptable salt comprises a sodium salt, a potassium salt, an ammonium salt, or any combination thereof.~~

~~118. The pharmaceutical composition of claim 116 or 117, which further comprises at least one additional therapeutic agent.~~

~~119. The pharmaceutical composition of claim 118, wherein the additional therapeutic agent is an STAT6 antagonist.~~

~~120. The pharmaceutical composition of claim 119, wherein the STAT6 antagonist is a chemical compound, an siRNA, an shRNA, an antisense oligonucleotide, a protein, or any combination thereof.~~

~~121. The pharmaceutical composition of claim 119 or 120, wherein the STAT6 antagonist is an anti-STAT6 antibody or a fragment thereof.~~

~~122. The pharmaceutical composition of claim 119 or 120, wherein the STAT6 antagonist comprises an antisense oligonucleotide (ASO).~~

~~123~~47. A kit comprising the extracellular vesicle of any one of claims 1 to ~~88~~ 42 and ~~115~~45, the ASO of claim 43~~any one of claims 89 to 112~~, the conjugate of claim 44~~113 or 114~~, or the pharmaceutical composition of claim 46~~any one of claims 116 to 122~~, and instructions for use.

~~124~~48. A diagnostic kit comprising the extracellular vesicle of any one of claims 1 to ~~88~~ 42 and ~~115~~45, the ASO of claim 43~~any one of claims 89 to 112~~, the conjugate of claim 44~~113 or 114~~, or the pharmaceutical composition of ~~any one of claims 116 to 122~~claim 46, and instructions for use.

~~125. A method of inhibiting or reducing STAT6 protein expression in a cell, comprising administering the extracellular vesicle of any one of claims 1 to 88 and 115, the ASO of any one of claims 89 to 112, the conjugate of claim 113 or 114, or the pharmaceutical composition of any one of claims 116 to 122 to the cell expressing STAT6 protein, wherein the STAT6 protein expression in the cell is inhibited or reduced after the administration.~~

~~126. A method of treating a cancer in a subject in need thereof, comprising administering an effective amount of the extracellular vesicle of any one of claims 1 to 88 and 115, the ASO of any one of claims 89 to 112, the conjugate of claim 113 or 114, or the pharmaceutical composition of any one of claims 116 to 122 to the subject.~~

~~127~~49. Use of the extracellular vesicle of any one of claims 1 to ~~88~~ 42 and ~~115~~45, the ASO of claim 43~~any one of claims 89 to 112~~, the conjugate of claim 44~~113 or 114~~, or the pharmaceutical

composition of ~~any one of claims 116 to 122~~claim 46 in the manufacture of a medicament for the treatment of a cancer in a subject in need thereof.

~~128. The extracellular vesicle of any one of claims 1 to 88 and 115, the ASO of any one of claims 89 to 11243, the conjugate of claim 113 or 114, or the pharmaceutical composition of any one of claims 116 to 122 for use in the treatment of a cancer in a subject in need thereof.~~

~~129. A method of treating a disease or disorder in a subject in need thereof, comprising administering an effective amount of the extracellular vesicle of any one of claims 1 to 88 and 115, the ASO of any one of claims 89 to 112, the conjugate of claim 113 or 114, or the pharmaceutical composition of any one of claims 116 to 122 to the subject, wherein the disease or disorder is selected from a fibrosis, an inflammation, a neurodegenerative disease, a metabolic disorder/CVD, and any combination thereof.~~

~~13050~~. Use of the extracellular vesicle of any one of claims 1 to ~~88~~ 42 and ~~115~~45, the ASO of claim 43~~any one of claims 89 to 112~~, the conjugate of claim 44~~113 or 114~~, or the pharmaceutical composition of ~~any one of claims 116 to 122~~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.

~~131. The extracellular vesicle of any one of claims 1 to 88 and 115, the ASO of any one of claims 89 to 112, the conjugate of claim 113 or 114, or the pharmaceutical composition of any one of claims 116 to 122 for use in 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.~~

~~132. The method of any one of claims 125, 126, and 129, the use of claim 127 or 130, or the compositions for use of claim 128 or 131, wherein the ASO inhibits or reduces expression of STAT6 mRNA in the cell after the administration.~~

~~133. The method, use, or composition for use of claim 132, wherein a level of STAT6 mRNA is reduced by at least about 20%, at least about 30%, at least about 40%, at least about 50%, at~~

least about 60%, at least about 70%, at least about 80%, at least about 90%, or about 100% after the administration compared to the level of STAT6 mRNA in a cell not exposed to the ASO.

134. The method of any one of claims 125 ,126, and 129, the use of claim 127 or 130, or the compositions for use of claim 128 or 131, wherein the expression of STAT6 protein is reduced by at least about 60%, at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 96%, at least about 97%, at least about 98%, at least about 99%, or about 100% after the administration compared to the expression of STAT6 protein in a cell not exposed to the ASO.

135. The method of any one of claims 125 ,126, and 129, the use of claim 127 or 130, or the compositions for use of claim 128 or 131, wherein the extracellular vesicle, the ASO, the conjugate, or the pharmaceutical composition is administered intracardially, orally, parenterally, intrathecally, intra-cerebroventricularly, pulmorarily, topically, or intraventricularly.

136. The method of claim 126, the use of claim 127, or the composition for use of claim 128, wherein the cancer is selected from the group consisting of fibrosarcoma, myxosarcoma, liposarcoma, chondrosarcoma, osteogenic sarcoma, chordoma, angiosarcoma, endotheliosarcoma, lymphangiosarcoma, lymphangioendotheliosarcoma, synovioma, mesothelioma, Ewing's tumor, leiomyosarcoma, rhabdomyosarcoma, colon carcinoma, pancreatic cancer, breast cancer, ovarian cancer, prostate cancer, squamous cell cancer, squamous cell cancer of the head and neck cancer, colorectal cancer, lymphoma, leukemia, liver cancer, glioblastoma, melanoma, myeloma basal cell cancer, adenocarcinoma, sweat gland cancer, sebaceous gland cancer, papillary cancer, papillary adenocarcinomas, cystadenocarcinoma, medullary cancer, bronchogenic cancer, renal cell cancer, hepatoma, bile duct cancer, choriocarcinoma, seminoma, embryonal cancer, Wilms' tumor, cervical cancer, testicular cancer, lung cancer, small cell lung cancer, bladder cancer, epithelial cancer, glioma, glioblastoma, astrocytoma, medulloblastoma, craniopharyngioma, ependymoma, pinealoma, hemangioblastoma, acoustic neuroma, oligodendroglioma, meningioma, melanoma, neuroblastoma, retinoblastoma, follicular lymphoma, Hodgkin's lymphoma, B cell lymphoma, and any combination thereof.

137. The method of claim 129, the use of claim 130, or the composition for use of claim 131, wherein the disease or disorder comprises a fibrosis.

~~138. The method of claim 129, the use of claim 130, or the composition for use of claim 131, wherein the disease or disorder comprises a fibrosis selected from the group consisting of liver fibrosis (NASH), cirrhosis, pulmonary fibrosis, cystic fibrosis, chronic ulcerative colitis/IBD, bladder fibrosis, kidney fibrosis, CAPS (Muckle-Wells syndrome), atrial fibrosis, endomyocardial fibrosis, old myocardial infarction, glial scar, arterial stiffness, arthrofibrosis, Crohn's disase, Dupuytren's contracture, keloid fibrosis, mediastinal fibrosis, myelofibrosis, Peyronie's disease, nephrogenic systemic fibrosis, progressive massive fibrosis, retroperitoneal fibrosis, scleroderma/systemic sclerosis, adhesive capsulitis, and any combination thereof.~~

~~139. A method of activating meningeal macrophages in a subject in need thereof, comprising administering the extracellular vesicle of any one of claims 1 to 88 and 115, the ASO of any one of claims 89 to 112, the conjugate of claim 113 or 114, or the pharmaceutical composition of any one of claims 116 to 122 to the subject.~~

~~140. A method of treating a cancer of the central nervous system in a subject in need thereof, comprising administering an effective amount of the extracellular vesicle of any one of claims 1 to 88 and 115, the ASO of any one of claims 89 to 112, the conjugate of claim 113 or 114, or the pharmaceutical composition of any one of claims 116 to 122 to the subject.~~

~~141. A method of inducing M1 polarization of meningeal macrophages in a subject in need thereof, comprising administering an effective amount of the extracellular vesicle of any one of claims 1 to 88 and 115, the ASO of any one of claims 89 to 112, the conjugate of claim 113 or 114, or the pharmaceutical composition of any one of claims 116 to 122 to the subject.~~

~~142. A method of inducing meningeal macrophage infiltration of a tumor in a subject in need thereof, comprising administering an effective amount of the extracellular vesicle of any one of claims 1 to 88 and 115, the ASO of any one of claims 89 to 112, the conjugate of claim 113 or 114, or the pharmaceutical composition of any one of claims 116 to 122 to the subject.~~