What is Claimed

1. An antisense oligonucleotide (ASO) comprising a contiguous nucleotide sequence ~~of~~ 10 to 30 nucleotides in length that are complementary to a nucleic acid sequence within a angiopoietin like 2 (*ANGPTL2*) transcript, wherein the ASO is a gapmer comprising one or more sugar modified nucleosides, and wherein the contiguous nucleotide sequence comprises the sequence set forth in any one of SEQ ID NO: 4 to SEQ ID NO: 193 or the sequence set forth in any one of SEQ ID NO: 4 to SEQ ID NO: 193 with one or two mismatches.

2. The ASO of claim 1, which 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 *ANGPTL2* transcript.

3. The ASO of claim 1 or 2, wherein the *ANGPTL2* transcript is selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 196, SEQ ID NO: 197, SEQ ID NO: 198, SEQ ID NO: 199, and SEQ ID NO: 207.

4. The ASO of any one of claims 1 to 3, wherein the ASO is capable of reducing ANGPTL2 protein expression in a human cell (*e.g.*, SK-N-AS cell) which is expressing the ANGPTL2 protein.

5. The ASO of claim 4, wherein the ANGPTL2 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 ANGPTL2 protein expression in a human cell that is not exposed to the ASO.

6. The ASO of any one of claims 1 to 5, which is capable of reducing *ANGPTL2* transcript (*e.g.*, mRNA) expression in a human cell (*e.g.*, SK-N-AS cell), which is expressing the *ANGPTL2* transcript.

7. The ASO of claim 6, wherein the *ANGPTL2* transcript 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 *ANGPTL2* transcript expression in a human cell that is not exposed to the ASO.

~~8. The ASO of any one of claims 1 to 7, wherein the ASO is a gapmer.~~

~~9. The ASO of claim 8, wherein the ASO comprises one or more nucleoside analogs.~~

~~10~~8. The ASO of claim ~~9~~1, wherein ~~the~~ one or more of the sugar modified nucleosides ~~nucleoside analogs~~ comprise 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; bicyclic nucleoside analog ~~(LNA)~~; or combinations thereof.

~~11~~9. The ASO of claim ~~9~~ 1 or ~~10~~8, wherein the one or more ~~nucleoside analogs are~~ of the sugar modified nucleosides is an affinity enhancing 2' sugar modified nucleoside.

~~12~~10. The ASO of claim ~~11~~9, wherein the affinity enhancing 2' sugar modified nucleoside is a locked nucleic acid (LNA)~~an LNA~~.

~~13~~11. The ASO of claim ~~12~~10, 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.

~~14~~12. The ASO of any one of claims 1 to ~~13~~11, wherein the ASO comprises one or more 5'-methyl-cytosine nucleobases.

~~15~~13. The ASO of any one of claims 1 to ~~14~~12, wherein the ASO is capable of (i) reducing *ANGPTL2* mRNA level in SK-N-AS cells; (ii) reducing ANGPTL2 protein level in SK-N-AS cells; (iii) reducing, ameliorating, or treating one or more symptoms of a disease or disorder associated with abnormal ANGPTL2 expression and/or activity, wherein the disease or disorder associated with abnormal ANGPTL2 expression and/or activity comprises a cardiovascular disease, obesity, metabolic disease, type 2 diabetes, cancers, an atherosclerosis, coronary artery disease, stroke, heart failure, hypertensive heart disease, rheumatic heart disease, cardiomyopathy, heart arrhythmia, congenital heart disease, valvular heart disease carditis, aortic aneurysms, peripheral artery disease, thromboembolic disease, venous thrombosis, comprises a left-sided heart failure, a right-sided heart failure, a congestive heart failure, a heart failure with reduced ejection fraction (HFrEF), a heart failure with preserved ejection fraction (HFpEF), a heart failure with mid-range ejection fraction (HFmrEF), a hypertrophic cardiomyopathy (HCM), a hypertensive heart disease (HHD), hypertensive hypertrophic cardiomyopathy or combinations thereof; or (iv) any combination thereof.

~~16. The ASO of claim 15, wherein the disease or disorder associated with abnormal ANGPTL2 expression and/or activity comprises a cardiovascular disease, obesity, metabolic disease, type 2 diabetes, cancers, or combinations thereof.~~

~~17~~14. The ASO of any one of claims 1 to ~~16~~13, wherein the contiguous nucleotide sequence is complementary to a nucleic acid sequence comprising (i) nucleotides 1 – 211 of SEQ ID NO: 1;

(ii) nucleotides 471 – 686 of SEQ ID NO: 1; (iii) nucleotides 1,069 – 1,376 of SEQ ID NO: 1; (iv) nucleotides 1,666 – 8,673 of SEQ ID NO: 1; (v) nucleotides 8,975 – 12,415 of SEQ ID NO: 1; (vi) nucleotides 12,739 – 18,116 of SEQ ID NO: 1; (vii) nucleotides 18,422 – 29,875 of SEQ ID NO: 1; or (viii) nucleotides 30,373 – 35,389 of SEQ ID NO: 1.

~~18~~15. The ASO of any one of claims 1 to ~~17~~14, wherein the contiguous nucleotide sequence is complementary to a nucleic acid sequence comprising (i) nucleotides 37 - 161 of SEQ ID NO: 1; (ii) nucleotides 521 - 636 of SEQ ID NO: 1; (iii) nucleotides 1,119 – 1,326 of SEQ ID NO: 1; (iv) nucleotides 1,716 – 8,623 of SEQ ID NO: 1; (v) nucleotides 9,025 – 12,365 of SEQ ID NO: 1; (vi) nucleotides 12,789 – 18,066 of SEQ ID NO: 1; (vii) nucleotides 18,472 – 29,825 of SEQ ID NO: 1; or (viii) nucleotides 30,423 – 35,339 of SEQ ID NO: 1.

~~19~~16. The ASO of any one of claims 1 to ~~18~~15, wherein the contiguous nucleotide sequence is complementary to a nucleic acid sequence comprising (i) nucleotides 87 – 111 of SEQ ID NO: 1; (ii) nucleotides 571 – 586 of SEQ ID NO: 1; (iii) nucleotides 1,169 – 1,276 of SEQ ID NO: 1; (iv) nucleotides 1,766 – 8,573 of SEQ ID NO: 1; (v) nucleotides 9,075 – 12,315 of SEQ ID NO: 1; (vi) nucleotides 12,839 – 18,016 of SEQ ID NO: 1; (vii) nucleotides 18,522 – 29,775 of SEQ ID NO: 1; or (viii) nucleotides 30,473 – 35,289 of SEQ ID NO: 1.

~~20~~17. The ASO of any one of claims 1 to ~~19~~16, wherein the contiguous nucleotide sequence is complementary to a nucleic acid comprising nucleotides 20,187 – 20,234 of SEQ ID NO: 1.

~~21~~18. The ASO of any one of claims 1 to ~~20~~17, wherein the contiguous nucleotide sequence is complementary to a nucleic acid comprising nucleotides 20,202 – 20,219 of SEQ ID NO: 1.

~~22~~19. The ASO of any one of claims 1 to ~~21~~18, wherein the contiguous nucleotide sequence comprises SEQ ID NO: 4 to SEQ ID NO: 193 with one or two mismatches.

~~23~~20. The ASO of any one of claims 1 to ~~21~~18, wherein the contiguous nucleotide sequence comprises the nucleotide sequence selected from the sequences in FIG. 2 (SEQ ID NO: 4 to SEQ ID NO: 193).

~~24~~21. The ASO of any one of claims 1 to ~~23~~20, wherein the contiguous nucleotide sequence comprises SEQ ID NO: 8, SEQ ID NO: 20, SEQ ID NO: 38, SEQ ID NO: 46, SEQ ID NO: 79, SEQ ID NO: 84, SEQ ID NO: 82, SEQ ID NO: 88, SEQ ID NO: 85, SEQ ID NO: 90, SEQ ID NO: 89, SEQ ID NO: 93, SEQ ID NO: 95, SEQ ID NO: 97, SEQ ID NO: 101, SEQ ID NO: 111, SEQ ID NO: 116, SEQ ID NO: 120, SEQ ID NO: 121, SEQ ID NO: 122, SEQ ID NO: 132, SEQ ID NO: 142, SEQ ID NO: 141, SEQ ID NO: 143, SEQ ID NO: 144, or SEQ ID NO: 146.

~~25~~22. The ASO of any one of claims 1 to ~~23~~20, wherein the contiguous nucleotide sequence comprises SEQ ID NO: 141, SEQ ID NO: 122, SEQ ID NO: 8, SEQ ID NO: 38, SEQ ID NO: 95, SEQ ID NO: 88, or SEQ ID NO: 120.

~~26~~23. The ASO of any one of claims 1 to ~~23~~20, wherein the contiguous nucleotide sequence comprises SEQ ID NO: 116, SEQ ID NO: 118, SEQ ID NO: 117, SEQ ID NO: 120, SEQ ID NO: 119, SEQ ID NO: 121, SEQ ID NO: 122, or combinations thereof.

~~27~~24. The ASO of any one of claims 1 to ~~26~~23, which has a design selected from the group consisting of the designs in FIG. 2, wherein the upper letter is a sugar modified nucleoside and the lower case letter is DNA.

~~28~~25. The ASO of any one of claims 1 to ~~27~~24, which has from 15 to 20 nucleotides in length.

~~29~~26. The ASO of any one of claims 1 to ~~28~~25, wherein the contiguous nucleotide sequence comprises one or more modified internucleoside linkage.

~~30~~27. The ASO of claim ~~29~~26, wherein the one or more modified internucleoside linkage is a phosphorothioate linkage.

~~31~~28. The ASO of claim ~~29~~ 26 or ~~30~~27, wherein at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or 100% of internucleoside linkages are modified.

~~32~~29. The ASO of claim 28~~31~~, wherein each of the internucleoside linkages is a phosphorothioate linkage.

~~33~~30. A conjugate comprising the ASO of any one of claims 1 to 29~~32~~, wherein the ASO is covalently attached to at least one non-nucleotide or non-polynucleotide moiety.

~~34~~31. The conjugate of claim ~~33~~30, 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.

~~35~~32. A pharmaceutical composition comprising the ASO of any one of claims 1 to ~~32~~ 29 or the conjugate of claim ~~33~~ 30 or ~~34~~31, and a pharmaceutically acceptable diluent, carrier, salt, or adjuvant.

~~36~~33. The pharmaceutical composition of claim ~~35~~32, wherein the pharmaceutically acceptable salt comprises a sodium salt, a potassium salt, an ammonium salt, or any combination thereof.

~~37~~34. The pharmaceutical composition of claim ~~35~~ 32 or ~~36~~33, which further comprises at least one further therapeutic agent.

3835. The pharmaceutical composition of claim 3734, wherein the further therapeutic agent is a ANGPTL2 antagonist.

3936. The pharmaceutical composition of claim 3835, wherein the ANGPTL2 antagonist is an anti-ANGPTL2 antibody or fragment thereof.

4037. A kit comprising the ASO of any one of claims 1 to 3229, the conjugate of claim 33 30 or 3431, or the pharmaceutical composition of any one of claims 35 32 to 3936, and instructions for use.

4138. A diagnostic kit comprising the ASO of any one of claims 1 to 2932, the conjugate of claim 303 or 314, or the pharmaceutical composition of any one of claims 352 to 369, and instructions for use.

~~42. A method of inhibiting or reducing ANGPTL2 protein expression in a cell, comprising administering the ASO of any one of claims 1 to 32, the conjugate of claim 33 or 34, or the pharmaceutical composition of any one of claims 35 to 39 to the cell expressing ANGPTL2 protein, wherein the ANGPTL2 protein expression in the cell is inhibited or reduced after the administration.~~

4339. An *in vitro* method of inhibiting or reducing ANGPTL2 protein expression in a cell, comprising contacting the ASO of any one of claims 1 to 2932, the conjugate of claim 33 30 or 3431, or the pharmaceutical composition of any one of claims 35 32 to 39 36 to the cell expressing ANGPTL2 protein, wherein the ANGPTL2 protein expression in the cell is inhibited or reduced after the contacting.

4440. The method of claim 42 39or 43, wherein the ASO inhibits or reduces expression of *ANGPTL2* transcript (*e.g.*, mRNA) in the cell after the administration or after the contacting.

4541. The method of claim 4440, wherein the expression of *ANGPTL2* transcript (*e.g.*, 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 a cell not exposed to the ASO.

4642. The method of any one of claims 42 to 4539 to 41, wherein the expression of ANGPTL2 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 a cell not exposed to the ASO.

4743. The method of any one of claims 39 to 4242 to 46, wherein the cell is a brain cell, *e.g.*, neuroblast (*e.g.*, SK-N-AS cell).

~~48~~44. Use of the ASO of any one of claims 1 to ~~32~~29, the conjugate of claim ~~33~~ 30 or ~~34~~31, or the pharmaceutical composition of any one of claims ~~35~~ 32 to ~~39~~ 36 in the manufacture of a medicament for reducing, ameliorating, or treating one or more symptoms of a disease or disorder associated with abnormal ANGPTL2 expression and/or activity in a subject in need thereof, wherein the medicament comprises an effective amount of the ASO, the conjugate, or the pharmaceutical composition ~~is to be administered to the subject~~, and wherein, the disease or disorder associated with abnormal ANGPTL2 expression and/or activity comprises a cardiovascular disease, obesity, metabolic disease, type 2 diabetes, cancers, an atherosclerosis, coronary artery disease, stroke, heart failure, hypertensive heart disease, rheumatic heart disease, cardiomyopathy, heart arrhythmia, congenital heart disease, valvular heart disease carditis, aortic aneurysms, peripheral artery disease, thromboembolic disease, venous thrombosis, comprises a left-sided heart failure, a right-sided heart failure, a congestive heart failure, a heart failure with reduced ejection fraction (HFrEF), a heart failure with preserved ejection fraction (HFpEF), a heart failure with mid-range ejection fraction (HFmrEF), a hypertrophic cardiomyopathy (HCM), a hypertensive heart disease (HHD), hypertensive hypertrophic cardiomyopathy or combinations thereof.

~~49~~45. Use of the ASO of any one of claims 1 to ~~32~~ 29, the conjugate of claim ~~33~~ 30 or ~~34~~31, or the pharmaceutical composition of any one of claims ~~35~~ 32 to ~~39~~ 36 in~~for~~ the manufacture of a medicament for reducing, ameliorating, or treating one or more symptoms of a disease or disorder associated with abnormal ANGPTL2 expression and/or activity in a subject in need thereof, wherein the disease or disorder associated with abnormal ANGPTL2 expression and/or activity comprises a cardiovascular disease, obesity, metabolic disease, type 2 diabetes, cancers, an atherosclerosis, coronary artery disease, stroke, heart failure, hypertensive heart disease, rheumatic heart disease, cardiomyopathy, heart arrhythmia, congenital heart disease, valvular heart disease carditis, aortic aneurysms, peripheral artery disease, thromboembolic disease, venous thrombosis, comprises a left-sided heart failure, a right-sided heart failure, a congestive heart failure, a heart failure with reduced ejection fraction (HFrEF), a heart failure with preserved ejection fraction (HFpEF), a heart failure with mid-range ejection fraction (HFmrEF), a hypertrophic cardiomyopathy (HCM), a hypertensive heart disease (HHD), hypertensive hypertrophic cardiomyopathy or combinations thereof.

~~50~~46. Use of the ASO of any one of claims 1 to ~~32~~29, the conjugate of claim ~~33~~ 30 or ~~34~~31, or the pharmaceutical composition of any one of claims ~~35~~ 32 to ~~39~~ 36 in~~for~~ the manufacture of a medicament for the treatment of a disease or disorder associated with abnormal ANGPTL2

expression and/or activity in a subject in need thereof, wherein the disease or disorder associated with abnormal ANGPTL2 expression and/or activity comprises a cardiovascular disease, obesity, metabolic disease, type 2 diabetes, cancers, an atherosclerosis, coronary artery disease, stroke, heart failure, hypertensive heart disease, rheumatic heart disease, cardiomyopathy, heart arrhythmia, congenital heart disease, valvular heart disease carditis, aortic aneurysms, peripheral artery disease, thromboembolic disease, venous thrombosis, comprises a left-sided heart failure, a right-sided heart failure, a congestive heart failure, a heart failure with reduced ejection fraction (HFrEF), a heart failure with preserved ejection fraction (HFpEF), a heart failure with mid-range ejection fraction (HFmrEF), a hypertrophic cardiomyopathy (HCM), a hypertensive heart disease (HHD), hypertensive hypertrophic cardiomyopathy or combinations thereof.

~~51~~47. The ASO of any one of claims 1 to ~~32~~29, the conjugate of claim ~~33~~ 30 or ~~34~~31, or the pharmaceutical composition of any one of claims ~~35~~ 32 to ~~39~~ 36 for use in therapy.

~~52~~48. The ASO of any one of claims 1 to ~~32~~29, the conjugate of claim ~~33~~ 30 or ~~34~~31, or the pharmaceutical composition of any one of claims ~~35~~ 32 to ~~39~~ 36 for use in therapy of a disease or disorder associated with abnormal ANGPTL2 expression and/or activity in a subject in need thereof, wherein the disease or disorder associated with abnormal ANGPTL2 expression and/or activity comprises a cardiovascular disease, obesity, metabolic disease, type 2 diabetes, cancers, an atherosclerosis, coronary artery disease, stroke, heart failure, hypertensive heart disease, rheumatic heart disease, cardiomyopathy, heart arrhythmia, congenital heart disease, valvular heart disease carditis, aortic aneurysms, peripheral artery disease, thromboembolic disease, venous thrombosis, comprises a left-sided heart failure, a right-sided heart failure, a congestive heart failure, a heart failure with reduced ejection fraction (HFrEF), a heart failure with preserved ejection fraction (HFpEF), a heart failure with mid-range ejection fraction (HFmrEF), a hypertrophic cardiomyopathy (HCM), a hypertensive heart disease (HHD), hypertensive hypertrophic cardiomyopathy or combinations thereof.

~~53. The ASO of claim 15, the use of any one of claims 48 to 50, or the ASO for use of claim 52, wherein the disease or disorder associated with abnormal ANGPTL2 expression and/or activity comprises a cardiovascular disease, obesity, metabolic disease, type 2 diabetes, cancers, or combinations thereof.~~

~~54. The ASO, use, or ASO for use of claim 53, wherein the cardiovascular disease or disorder comprises an atherosclerosis, coronary artery disease, stroke, heart failure, hypertensive heart disease, rheumatic heart disease, cardiomyopathy, heart arrhythmia, congenital heart disease,~~

~~valvular heart disease carditis, aortic aneurysms, peripheral artery disease, thromboembolic disease, venous thrombosis, or any combination thereof.~~

~~55. The ASO, use, or ASO for use of claim 54, wherein the cardiovascular disease or disorder is heart failure.~~

~~56. The ASO, use, or ASO for use of claim 55, wherein the heart failure comprises a left-sided heart failure, a right-sided heart failure, a congestive heart failure, a heart failure with reduced ejection fraction (HFrEF), a heart failure with preserved ejection fraction (HFpEF), a heart failure with mid-range ejection fraction (HFmrEF), a hypertrophic cardiomyopathy (HCM), a hypertensive heart disease (HHD), or hypertensive hypertrophic cardiomyopathy.~~

~~57~~49. The use of any one of claims ~~48 to 50~~44 to 46~~ and 53 to 56~~, or the ASO for use of ~~any one of claims 52 to 56~~claim 47 or 48, wherein the subject is a human.

~~58~~50. The use of any one of claims~~ 48 to 50 and 53 to 57~~44 to 46, or the ASO for use of any one of claims 47~~52~~ to 49~~57~~, wherein the ASO, the conjugate, or the pharmaceutical composition is to be administered intracardially, orally, parenterally, intrathecally, intracerebroventricularly, pulmonarily, topically, or intraventricularly.