

WHAT IS CLAIMED IS:

1. A multimeric oligonucleotide comprising a plurality of subunits ***** and a protected sulfur-containing end group,

wherein:

each of the subunits ***** is independently a single or double stranded oligonucleotide and is joined to another subunit by a covalent linker ●;

at least one of the covalent linker ● is a sulfur-containing covalent linker ◇, optionally the sulfur-containing covalent linker comprises a sulfur-containing cleavable group;

the sulfur-containing end group is deprotectable under a deprotection condition;

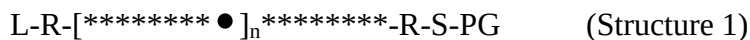
and

each sulfur-containing covalent linker ◇ is stable under the deprotection condition.

2. The multimeric oligonucleotide of claim 1, wherein at least one sulfur-containing covalent linker ◇ comprises a cleavable group, optionally a sulfur-containing cleavable group, that is cleavable under a cleavage condition that is not the deprotection condition.

3. The multimeric oligonucleotide of any one of claims 0 to 2, wherein the protected sulfur-containing end group comprises a protected thiol group.

4. The multimeric oligonucleotide of any one of claims 0 to 3 comprising the following Structure 1:



wherein:

L is a bioactive moiety that may be present or absent;

each R is individually a spacer group that may be present or absent;

each ***** is independently a single or double stranded oligonucleotide subunit;

each ● is a covalent linker joining adjacent oligonucleotide subunits;

n is an integer in the range of 1 to 9;

S-PG is a protected sulfur-containing end group, optionally a protected thiol group, that is deprotectable under a deprotection condition; and

at least one $\bullet$ is a sulfur-containing covalent linker $\diamond$, optionally the sulfur-containing covalent linker comprises a sulfur-containing cleavable group, that is stable under the deprotection condition.

5. The multimeric oligonucleotide of claim 4, wherein at least one of the spacer groups R that is present in the multimeric oligonucleotide comprises alkyl, alkyl ether, ester, aryl, heteroaryl, heterocyclyl, alkyl-aryl, alkyl-heteroaryl, or alkyl-heterocyclyl; optionally wherein every spacer group R that is present in the multimeric oligonucleotide comprises alkyl, alkyl ether, ester, aryl, heteroaryl, heterocyclyl, alkyl-aryl, alkyl-heteroaryl, or alkyl-heterocyclyl.

6. The multimeric oligonucleotide of any one of claims 1 to 5, wherein the sulfur-containing covalent linker $\diamond$ comprises a linkage represented by $-\mathbf{R}^1-\mathbf{R}^2-\mathbf{R}^1-$, wherein:

each $\mathbf{R}^1$ is individually absent or a spacer group; and

$\mathbf{R}^2$ is a thiopropionate or disulfide group.

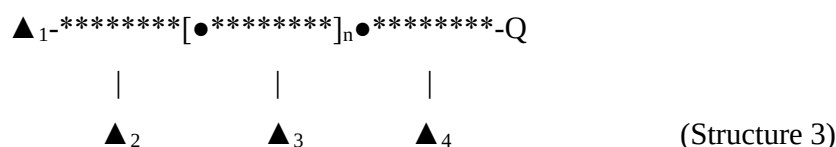
7. The multimeric oligonucleotide of claim 6, wherein at least one of the spacer groups $\mathbf{R}^1$ that is present in the linkage comprises alkyl, alkyl ether, ester, aryl, heteroaryl, heterocyclyl, alkyl-aryl, alkyl-heteroaryl, or alkyl-heterocyclyl; optionally wherein every spacer group $\mathbf{R}^1$ that is present in the linkage comprises alkyl, alkyl ether, ester, aryl, heteroaryl, heterocyclyl, alkyl-aryl, alkyl-heteroaryl, or alkyl-heterocyclyl.

8. The multimeric oligonucleotide of any one of claim 6 or 7, wherein at least one of the spacer groups $\mathbf{R}^1$ that is present in the linkage comprises a phosphate linking group, a phosphorothioate linking group, a phosphonate linking group, or a dithiophosphate linking group; optionally wherein every spacer group $\mathbf{R}^1$ that is present in the linkage comprises a phosphate linking group, a phosphorothioate linking group, a phosphonate linking group, or a dithiophosphate linking group.

9. The multimeric oligonucleotide of any one of claims 1 to 8, wherein the protected sulfur-containing end group comprises a protecting group selected from optionally substituted alkyl, optionally substituted alkoxyalkyl, optionally substituted trialkylsilyl, optionally substituted arylalkylsilyl, optionally substituted aryl, optionally substituted benzyl, optionally substituted acyl and optionally substituted benzoyl.

10. The multimeric oligonucleotide of any one of claims 1 to 8, wherein the protected sulfur-containing end group comprises a protecting group PG selected from trityl, methoxytrityl, dimethoxytrityl, methylmethoxy, triisopropylsilyl, dinitrophenyl, nitrophenyl, acetyl and benzoyl.

11. A multi-conjugate comprising a plurality of subunits ***** joined to one another by one or more covalent linkers ●, wherein the multi-conjugate comprises Structure 3:



wherein:

each of the subunits ***** is independently a bioactive moiety;

at least one covalent linker ● is a sulfur-containing covalent linker ◇, optionally the sulfur-containing covalent linker ◇ comprises a sulfur-containing cleavable group ;

each of $\blacktriangle_1$, $\blacktriangle_2$, $\blacktriangle_3$, and $\blacktriangle_4$ is a group that is independently absent or comprises a functional moiety joined to a subunit and, optionally, a spacer group joining the functional moiety to the subunit;

Q is a group that comprises a sulfur-containing end group, and optionally a spacer group joining Q to the subunit; and

n is an integer greater than or equal to zero; optionally n is an integer in the range of 0 to 10; optionally n is an integer in the range of 0 to 10; optionally n is an integer in the range of 1 to 4; optionally, n is 1, 2, 3 or 4.

12. The multi-conjugate of claim 11, wherein at least one of the subunits ***** present in Structure 3 is not an oligonucleotide.

13. The multi-conjugate of claim 11 or 12, wherein at least one of the subunits
***** present in Structure 3 comprises an oligopeptide or a protein.

14. The multi-conjugate of any one of claims 11 to 13, wherein at least one functional moiety is present.

15. The multi-conjugate of claim 14, wherein the at least one functional moiety that is present is a targeting ligand.

16. A composition comprising a multimeric oligonucleotide of any one of claims 1 to 10 and a pharmaceutically acceptable excipient.

17. A composition comprising a multi-conjugate of any one of claims 11 to 15 and a pharmaceutically acceptable excipient.

18. Use of a multimeric oligonucleotide of any one of claims 1 to 10 in the manufacture of a medicament.

19. Use of a multi-conjugate of any one of claims 11 to 15 in the manufacture of a medicament.

20. The multimeric oligonucleotide of any one of claims 1 to 10 for use in modulating activity of a target gene in a cell.

21. The multi-conjugate of any one of claims 11 to 15 for use in observing the activity of a bioactive moiety in a cell.