CLAIMS

1. An siRNA molecule comprising a sense strand and an antisense strand, wherein the antisense strand comprises a nucleic acid comprising:

(a) a 5’ end and a 3’ end;

(b) a seed region that is complementary to a region of a gene comprising an allelic polymorphism;

(c) a single nucleotide polymorphism (SNP) position nucleotide that is complementary to the allelic polymorphism;

(d) a mismatch (MM) position nucleotide that is a mismatch with a nucleotide in the gene;

(e) at least three 2’-fluoro-ribonucleotides located within four, three or two nucleotides from the SNP position nucleotide; and

(f) at least three 2’-methoxy-ribonucleotides located within four, three or two nucleotides from the MM position nucleotide; and

(g) wherein a 2’-fluoro-ribonucleotide is positioned immediately 3’ to the SNP position nucleotide.

2. The siRNA molecule of claim 1, wherein a 2’-methoxy-ribonucleotide is positioned immediately 5’ to the MM position nucleotide and/or a 2’-methoxy-ribonucleotide is positioned immediately 3’ to the MM position nucleotide.

3. The siRNA molecule of claim 2, wherein the SNP position nucleotide is present in a seed region, and wherein the MM position nucleotide is located 2-11 nucleotides from the SNP position nucleotide.

4. The siRNA molecule of claim 3, wherein the SNP position nucleotide is present from position 2 to position 6 from the 5’ end, and wherein the MM position nucleotide is located 2-6 nucleotides from the SNP position nucleotide.