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Figure 1



(57) Abstract: This invention relates to compounds, compositions, and methods useful for reducing EGFR target RNA and protein levels via use of dsRNAs, e.g., Dicer substrate siRNA (DsiRNA) agents.

METHODS AND COMPOSITIONS FOR THE SPECIFIC INHIBITION OF EGFR BY DOUBLE-STRANDED RNA

CROSS-REFERENCE TO RELATED APPLICATIONS

The present application claims priority to, and the benefit under 35 U.S.C. §119(e) of, U.S. provisional patent application No. 61/478,093, filed April 22, 2011, entitled “Methods and Compositions for the Specific Inhibition of EGFR by Double-Stranded RNA”. The entire teachings of this application are incorporated herein by reference.

FIELD OF THE INVENTION

The present invention relates to compounds, compositions, and methods for the study, diagnosis, and treatment of traits, diseases and conditions that respond to the modulation of EGFR gene expression and/or activity.

BACKGROUND OF THE INVENTION

Cell proliferation and programmed cell death are critical to growth, development and maintenance of an organism. In proliferative diseases such as cancer, the processes of cell proliferation and/or programmed cell death are often perturbed. For example, a cancer cell may have unregulated cell division *via* overexpression of a positive regulator of the cell cycle or *via* loss of a negative regulator of the cell cycle, perhaps by mutation. Alternatively, a cancer cell may have lost the ability to undergo programmed cell death through the overexpression of a negative regulator of apoptosis. Accordingly, there is a need to develop new therapeutic agents that will target cancer-associated genes (e.g., oncogenes) in a manner capable of modulating such targets and, ideally, restoring the processes of checkpoint control and programmed cell death to cancerous cells.

The EGFR gene that encodes for the epidermal growth factor receptor (EGFR; ErbB-1; HER1 in humans) is the cell-surface receptor for members of the epidermal growth factor family (EGF-family) of extracellular protein ligands (Herbst RS. *Int. J. Radiat. Oncol. Biol. Phys.* 59 (2 Suppl): 21–6). The epidermal growth factor receptor is a member of the ErbB family of receptors, a subfamily of four closely related receptor tyrosine kinases: EGFR (ErbB-1), HER2/c-neu (ErbB-2), Her 3 (ErbB-3) and Her 4 (ErbB-4). Mutations affecting EGFR expression or activity have been associated with cancer (Zhang *et al. J. Clin. Invest.* 117: 2051–8). EGFR is a glycoprotein with a molecular weight of 170,000 to 180,000 and is an intrinsic tyrosine-specific protein kinase, which is stimulated upon epidermal growth

factor (EGF) binding. The known downstream effectors of EGFR include PI3-K, RAS-RAF-MAPK P44/P42, and protein kinase C signaling pathways. EGFR signaling is involved in cell growth, angiogenesis, DNA repair, and autocrine growth regulation in a wide spectrum of human cancer cells (Wakeling A E., *Curr Opin Pharmacol* 2002, 2: 382-387). Therefore, it has emerged as a target for the development of new cancer therapies. Recently, a monoclonal antibody against EGFR called cetuximab has been developed, which has shown excellent clinical effects for the treatment of lung, colorectal, and head and neck cancers in clinical trials in humans (e.g., Shin *et al.*, *Clin Cancer Res*, 2001, 7:1204-1213). Specifically, cetuximab is indicated for treatment of subjects/patients with the following forms of cancer: EGFR expressing, KRAS wild-type metastatic colorectal cancer in combination with chemotherapy or as a single agent in patients who have failed in oxaliplatin- or irinotecan-based therapy and who are intolerant to irinotecan; squamous cell carcinoma of the head and neck (SCCHN) in combination with radiation therapy, or as a single agent in patients who have had prior platinum-based therapy (two studies have evaluated the benefits of cetuximab in patients with SCCHN in both the locally advanced and the recurrent and/or metastatic settings, with the latter trial being a Phase III trial that demonstrated a survival benefit in first-line recurrent and/or metastatic disease). Other small chemical inhibitors of EGFR, such as ZD-1839 have also been developed and demonstrated antitumor effects *in vitro* and *in vivo* (Shawver L K, et al., *Cancer Cell* 2002, 1:117-123). However, clinical use of ZD-1839 in humans has not been very successful. (Baselga *Eur J Cancer* 2001, 37:S16-22).

Double-stranded RNA (dsRNA) agents possessing strand lengths of 25 to 35 nucleotides have been described as effective inhibitors of target gene expression in mammalian cells (Rossi *et al.*, U.S. Patent Application Nos. 2005/0244858 and US 2005/0277610). dsRNA agents of such length are believed to be processed by the Dicer enzyme of the RNA interference (RNAi) pathway, leading such agents to be termed "Dicer substrate siRNA" ("DsiRNA") agents. Additional modified structures of DsiRNA agents were previously described (Rossi *et al.*, U.S. Patent Application No. 2007/0265220).

BRIEF SUMMARY OF THE INVENTION

The present invention is directed to compositions that contain double stranded RNA ("dsRNA"), and methods for preparing them. The dsRNAs of the invention are capable of reducing the expression of a target EGFR gene in a cell, either *in vitro* or in a mammalian subject.

In one aspect, the invention provides an isolated double stranded nucleic acid (dsNA) having ribonucleotides and first and second nucleic acid strands and a duplex region of at least 25 base pairs, with the first strand of 25-34 nucleotides in length and the second strand of 26-35 nucleotides in length, where the second strand is sufficiently complementary to a target EGFR cDNA sequence of Table 13 along at least 15 nucleotides of the second oligonucleotide strand length to reduce EGFR target gene expression when the double stranded nucleic acid is introduced into a mammalian cell.

Another aspect of the invention provides an isolated double stranded nucleic acid (dsNA) having ribonucleotides and consisting of: (a) a sense region and an antisense region, where the sense region and the antisense region together form a duplex region consisting of 25-35 base pairs and the antisense region includes a sequence having at least 15 contiguous nucleotides that are complementary to a sequence of Table 17; and (b) from zero to two 3' overhang regions, where each overhang region is six or fewer nucleotides in length.

In another aspect, the invention provides an isolated dsNA having ribonucleotides, consisting of: (a) a sense region and an antisense region, where the sense region and the antisense region together form a duplex region consisting of 25-35 base pairs and the antisense region includes a sequence having at least 19 contiguous nucleotides that are complementary to a sequence of Tables 17 and 18; and (b) from zero to two 3' overhang regions, where each overhang region is six or fewer nucleotides in length.

In an additional aspect, the invention provides an isolated dsNA having ribonucleotides, consisting of: (a) a sense region and an antisense region, where the sense region and the antisense region together form a duplex region consisting of 25-35 base pairs and the antisense region includes a sequence that is the complement of a sequence of Tables 17-23; and (b) from zero to two 3' overhang regions, where each overhang region is six or fewer nucleotides in length.

In a further aspect, the invention provides an isolated dsNA having ribonucleotides, consisting of: (a) a sense region and an antisense region, where the sense region and the antisense region together form a duplex region consisting of 25-35 base pairs and the antisense region includes a sequence that is the complement of a sequence of Tables 17-23; and (b) from zero to two 3' overhang regions, where each overhang region is six or fewer nucleotides in length, and where, starting from the 5' end (position 1) of a EGFR mRNA sequence of Tables 17-26 (position 1), mammalian Ago2 cleaves the mRNA at a site between positions 9 and 10 of the sequence.

Another aspect of the invention provides an isolated dsNA having first and second nucleic acid strands having ribonucleotides and a duplex region of at least 25 base pairs, where the first strand is 25-34 nucleotides in length and includes a 5'-terminus and a 3'-terminus and the second strand of the dsNA is 26-35 nucleotides in length and includes a 5'-terminus and a 3'-terminus and includes 1-5 single-stranded nucleotides at its 3' terminus, where the second oligonucleotide strand is sufficiently complementary to a target EGFR mRNA sequence of Tables 17-26 or SEQ ID NOs: 2137-2396 along at least 19 nucleotides of the second oligonucleotide strand length to reduce EGFR target gene expression when the double stranded nucleic acid is introduced into a mammalian cell.

An additional aspect of the invention provides an isolated dsNA having first and second nucleic acid strands having ribonucleotides and a duplex region of at least 25 base pairs, where the first strand is 25-34 nucleotides in length and the second strand of the dsNA is 26-35 nucleotides in length and includes 1-5 single-stranded nucleotides at its 3' terminus, where the 3' terminus of the first oligonucleotide strand and the 5' terminus of the second oligonucleotide strand form a blunt end, and the second oligonucleotide strand is sufficiently complementary to a target EGFR sequence of Tables 17-26 or SEQ ID NOs: 2137-2396 along at least 19 nucleotides of the second oligonucleotide strand length to reduce EGFR mRNA expression when the double stranded nucleic acid is introduced into a mammalian cell.

In another aspect, the invention provides an isolated double stranded ribonucleic acid (dsNA) having first and second nucleic acid strands, where the dsNA includes a blunt end, where each of the first and second oligonucleotide strands consists of the same number of nucleotide residues and is at most 35 nucleotides in length, where the ultimate and penultimate residues of the 3' terminus of the first strand and the ultimate and penultimate residues of the 5' terminus of the second strand form one or two mismatched based pairs, where the second oligonucleotide strand is sufficiently complementary to a target EGFR cDNA sequence of Table 13 along at least 15 nucleotides of the second oligonucleotide strand length to reduce EGFR target gene expression when the double stranded nucleic acid is introduced into a mammalian cell, where the dsNA reduces EGFR mRNA levels by at least 70% when assayed *in vitro* in a mammalian cell at an effective concentration in the environment of the cell of 1 nanomolar or less.

In one embodiment, the dsNA reduces EGFR mRNA levels by at least 80% when assayed *in vitro* in a mammalian cell at an effective concentration of 1 nanomolar or less in

the environment of the cell. In another embodiment, the second strand is sufficiently complementary to a target EGFR cDNA sequence of Table 14 or, optionally, Table 15 along at least 15 nucleotides of the second strand length to reduce EGFR target gene expression when the double stranded nucleic acid is introduced into a mammalian cell. In an additional embodiment, the second strand is complementary to a target EGFR cDNA sequence of GenBank Accession Nos. NM_005228.3 and NM_207655.2 along at most 27 nucleotides of the second strand length.

In certain embodiments, the invention provides for an isolated dsNA wherein the first strand is 26-35 nucleotides in length, 27-35 nucleotides in length, 28-35 nucleotides in length, 29-35 nucleotides in length, 30-35 nucleotides in length, 31-35 nucleotides in length, 33-35 nucleotides in length, 34-35 nucleotides in length, 17-35 nucleotides in length, 19-35 nucleotides in length, 21-35 nucleotides in length, 23-35 nucleotides in length, 17-33 nucleotides in length, 17-31 nucleotides in length, 17-29 nucleotides in length, 17-27 nucleotides in length, 21-35 nucleotides in length or 19-33 nucleotides in length.

In related embodiments, the invention provides for an isolated dsNA wherein the second strand is 26-35 nucleotides in length, 27-35 nucleotides in length, 28-35 nucleotides in length, 29-35 nucleotides in length, 30-35 nucleotides in length, 31-35 nucleotides in length, 33-35 nucleotides in length, 34-35 nucleotides in length, 21-35 nucleotides in length, 23-35 nucleotides in length, 25-35 nucleotides in length, 27-35 nucleotides in length, 19-33 nucleotides in length, 19-31 nucleotides in length, 19-29 nucleotides in length, 19-27 nucleotides in length or 19-25 nucleotides in length.

In certain embodiments, the invention provides for an isolated dsNA, wherein each of said first and said second strands has a length which is at least 27 nucleotides, at least 28 nucleotides, at least 29 nucleotides, at least 30 nucleotides, at least 31 nucleotides, at least 32 nucleotides, at least 33 nucleotides, at least 34 nucleotides or at least 35 nucleotides.

The invention also provides for an isolated dsNA, wherein each of the first and the second strands has a length which is at least 27 and at most 30 nucleotides, at least 28 and at most 30 nucleotides and at least 29 and at most 30 nucleotides.

The invention provides for an isolated dsNA that is sufficiently complementary to a target EGFR mRNA sequence along at least 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25 or more nucleotides of the second oligonucleotide strand length to reduce EGFR target mRNA expression when the dsNA is introduced into a mammalian cell.

In one embodiment, the dsNA of the invention has a first oligonucleotide strand having a 5'-terminus and a 3'-terminus and a second oligonucleotide strand having a 5'-terminus and a 3'-terminus.

In one embodiment, the second strand includes a sequence of SEQ ID NOs: 357-616. In another embodiment, the first strand includes a sequence of SEQ ID NOs: 1-260, 1069-1328, 1781-2040 and 2137-2396. In one embodiment, the dsNA includes a pair of first strand/second strand sequences selected from Table 2, 3, 7 or 9.

In another embodiment, the second strand possesses 1-5 single-stranded nucleotides at its 3' terminus (referred to as a "3' overhang"). Optionally, the 3' overhang is 1-4, 1-3, 1-2 or a single nucleotide in length. In certain embodiments, the 3' overhang includes a modified nucleotide. Optionally, the modified nucleotide of the 3' overhang is a 2'-O-methyl ribonucleotide.

In one embodiment, the dsNA includes a modified nucleotide.

In one embodiment, the modified nucleotide residue(s) of the dsNA is 2'-O-methyl, 2'-methoxyethoxy, 2'-fluoro, 2'-allyl, 2'-O-[2-(methylamino)-2-oxoethyl], 4'-thio, 4'-CH₂-O-2'-bridge, 4'-(CH₂)₂-O-2'-bridge, 2'-LNA, 2'-amino or 2'-O-(N-methylcarbamate).

In another embodiment, all nucleotides of the 3' overhang are modified nucleotides.

In one embodiment, starting from the first nucleotide (position 1) at the 3' terminus of the first strand, position 1, 2 and/or 3 is substituted with a modified nucleotide. In a related embodiment, the modified nucleotide residue of the 3' terminus of the first strand is a deoxyribonucleotide, an acyclonucleotide or a fluorescent molecule. Optionally, position 1 of the 3' terminus of the first strand is a deoxyribonucleotide.

In certain embodiments, the 3' terminus of the first strand and the 5' terminus of the second strand form a blunt end.

In one embodiment, the first strand is 25 nucleotides in length and the second strand is 27 nucleotides in length.

In another embodiment, each of the first and the second strands is at least 26 nucleotides long.

In an additional embodiment, one or both of the first and second strands includes a 5' phosphate.

In one embodiment, starting from the 5' end of a EGFR mRNA sequence of Table 16 (position 1), mammalian Ago2 cleaves the mRNA at a site between positions 9 and 10 of the

sequence, thereby reducing EGFR target mRNA expression when the double stranded nucleic acid is introduced into a mammalian cell.

In a related embodiment, starting from the 5' end of a EGFR mRNA sequence of Table 6, mammalian Ago2 cleaves the mRNA at a site between positions 9 and 10 of the mRNA sequence, thereby reducing EGFR target mRNA expression when the double stranded nucleic acid is introduced into a mammalian cell.

In one embodiment, the second strand, starting from the nucleotide residue of the second strand that is complementary to the 5' terminal nucleotide residue of the first strand, possesses alternating modified and unmodified nucleotide residues. Optionally, the second strand, starting from the nucleotide residue of the second strand that is complementary to the 5' terminal nucleotide residue of the first strand, possesses unmodified nucleotide residues at all positions from position 18 to the 5' terminus of the second strand.

In one embodiment, each of the first strand and the second strand is 25-35 nucleotides in length. Optionally, each of the first and the second strands has a length which is at least 26 and at most 30 nucleotides.

In another embodiment, the second strand comprises a modification pattern as shown in Figure 4A. In a further embodiment, the second oligonucleotide strand includes a modification pattern selected from AS-M1 to AS-M46 and AS-M1* to AS-M46*.

Optionally, the first oligonucleotide strand includes a modification pattern selected from SM1 to SM22.

In one embodiment, the dsNA is cleaved endogenously in the cell by Dicer. Optionally, a nucleotide of the second or first strand is substituted with a modified nucleotide that directs the orientation of Dicer cleavage. In an additional embodiment, the orientation of Dicer cleavage is directed by the end structure of the dsNA (e.g., Dicer preferentially cleaves a 21mer of a blunt/overhang dsNA of the invention such that the overhang end is retained by the resultant preferred 21mer).

In another embodiment, the amount of the isolated double stranded nucleic acid sufficient to reduce expression of the target gene is 1 nanomolar or less, 200 picomolar or less, 100 picomolar or less, 50 picomolar or less, 20 picomolar or less, 10 picomolar or less, 5 picomolar or less, 2, picomolar or less, or even 1 picomolar or less in the environment of the cell.

In one embodiment, the isolated dsNA possesses greater potency than an isolated 21mer siRNA directed to the identical at least 15 nucleotides (or 19 nucleotides) of the target

EGFR cDNA in reducing target EGFR gene expression when assayed *in vitro* in a mammalian cell at an effective concentration of 1 nanomolar or less, 300 picomolar or less, 200 picomolar or less, 100 picomolar or less, 50 picomolar or less, 20 picomolar or less, 10 picomolar or less, 5 picomolar or less, 2, picomolar or less or even 1 picomolar or less in the environment of a cell.

In another embodiment, the isolated dsNA is sufficiently complementary to the target EGFR cDNA sequence to reduce EGFR target gene expression by at least 10%, at least 50%, at least 80-90%, at least 95%, at least 98%, or at least 99% when the double stranded nucleic acid is introduced into a mammalian cell.

In one embodiment, the first and second strands are joined by a chemical linker. Optionally, the 3' terminus of the first strand and the 5' terminus of the second strand are joined by a chemical linker.

In another embodiment, the dsNA possesses a deoxyribonucleotide, a dideoxyribonucleotide, an acyclonucleotide, a 3'-deoxyadenosine (cordycepin), a 3'-azido-3'-deoxythymidine (AZT), a 2',3'-dideoxyinosine (ddI), a 2',3'-dideoxy-3'-thiacytidine (3TC), a 2',3'-didehydro-2',3'-dideoxythymidine (d4T), a monophosphate nucleotide of 3'-azido-3'-deoxythymidine (AZT), a 2',3'-dideoxy-3'-thiacytidine (3TC) and a monophosphate nucleotide of 2',3'-didehydro-2',3'-dideoxythymidine (d4T), a 4-thiouracil, a 5-bromouracil, a 5-iodouracil, a 5-(3-aminoallyl)-uracil, a 2'-O-alkyl ribonucleotide, a 2'-O-methyl ribonucleotide, a 2'-amino ribonucleotide, a 2'-fluoro ribonucleotide, or a locked nucleic acid. Optionally, the dsNA possesses a phosphate backbone modification that is a phosphonate, a phosphorothioate or a phosphotriester. In one embodiment, the dsNA possesses a morpholino nucleic acid or a peptide nucleic acid (PNA).

In another embodiment, the second strand is sufficiently complementary to a target EGFR cDNA sequence of Table 13 along at least 19 nucleotides of the second strand length to reduce EGFR target gene expression when the double stranded nucleic acid is introduced into a mammalian cell.

In another aspect, the invention provides a method for reducing expression of a target EGFR gene in a mammalian cell involving contacting a mammalian cell *in vitro* with an isolated dsNA of the invention in an amount sufficient to reduce expression of a target EGFR gene in the cell. In one embodiment, target EGFR gene expression is reduced by at least 10%, at least 50% or at least 80-90%. Optionally, EGFR mRNA levels are reduced by at least 90% at least 8 days after the cell is contacted with the dsNA. In certain embodiments,

EGFR mRNA levels are reduced by at least 70% at least 10 days after the cell is contacted with the dsNA.

In a further aspect, the invention provides a method for reducing expression of a target EGFR gene in a mammal that involves administering an isolated dsNA of the invention to a mammal in an amount sufficient to reduce expression of a target EGFR gene in the mammal. Optionally, the isolated dsNA is administered at a dosage of 1 microgram to 5 milligrams per kilogram of the mammal per day, 100 micrograms to 0.5 milligrams per kilogram, 0.001 to 0.25 milligrams per kilogram, 0.01 to 20 micrograms per kilogram, 0.01 to 10 micrograms per kilogram, 0.10 to 5 micrograms per kilogram, or 0.1 to 2.5 micrograms per kilogram. In one embodiment, the administering step involves intravenous injection, intramuscular injection, intraperitoneal injection, infusion, subcutaneous injection, transdermal, aerosol, rectal, vaginal, topical, oral or inhaled delivery.

In another aspect, the invention provides a method for selectively inhibiting the growth of a cell that involves contacting a cell with an amount of an isolated dsNA of the invention sufficient to inhibit the growth of the cell. In one embodiment, the cell is a tumor cell of a subject. Optionally, wherein the cell is a tumor cell *in vitro*. In certain embodiments, the cell is a human cell. In certain embodiments, the tumor cell is a tumor cell of a subject. Optionally, the tumor cell is a non-small cell lung cancer cell. In certain embodiments, the non-small cell lung cancer cell is erlotinib resistant. In one embodiment, the non-small cell lung cancer cell does not comprise a KRAS mutation. Optionally, the growth of the cell is inhibited by an amount selected from the group consisting of at least 15%, at least 25%, at least 40% and at least 50%, as compared to an appropriate control.

In a further aspect, the invention provides a formulation that includes an isolated dsNA of the invention, where the dsNA is present in an amount effective to reduce target EGFR RNA levels when the dsNA is introduced into a mammalian cell *in vitro* by at least 10%, at least 50% or at least 80-90%, and the dsNA possesses greater potency than an isolated 21mer siRNA directed to the identical at least 15 nucleotides of the target EGFR cDNA in reducing target EGFR RNA levels when assayed *in vitro* in a mammalian cell at an effective concentration in the environment of a cell of 1 nanomolar or less. Optionally, the effective amount is 300 picomolar or less, 200 picomolar or less, 100 picomolar or less, 50 picomolar or less, 20 picomolar or less, 10 picomolar or less, 5 picomolar or less, 2, picomolar or less or 1 picomolar or less in the environment of the cell.

Another aspect of the invention provides a formulation that includes an isolated dsNA of the invention, where the dsNA is present in an amount effective to reduce target EGFR RNA levels when the dsNA is introduced into a cell of a mammalian subject by at least 10%, at least 50% or at least 80-90%, and the dsNA possesses greater potency than an isolated 21mer siRNA directed to the identical at least 15 nucleotides of the target EGFR cDNA in reducing target EGFR RNA levels when assayed *in vitro* in a mammalian cell at an effective concentration in the environment of a cell of 1 nanomolar or less. In one embodiment, the effective amount is a dosage of 1 microgram to 5 milligrams per kilogram of the subject per day, 100 micrograms to 0.5 milligrams per kilogram, 0.001 to 0.25 milligrams per kilogram, 0.01 to 20 micrograms per kilogram, 0.01 to 10 micrograms per kilogram, 0.10 to 5 micrograms per kilogram, or 0.1 to 2.5 micrograms per kilogram.

A further aspect of the invention provides a mammalian cell containing the isolated dsNA the invention.

Another aspect of the invention provides a pharmaceutical composition containing an isolated dsNA of the invention and a pharmaceutically acceptable carrier.

A further aspect of the invention provides a kit containing an isolated dsNA of the invention and instructions for its use.

Another aspect of the invention provides a composition possessing EGFR inhibitory activity consisting essentially of an isolated dsNA of the invention.

An additional aspect of the invention provides a composition possessing EGFR inhibitory activity consisting essentially of an isolated double stranded nucleic acid (dsNA) possessing first and second nucleic acid strands, where the first strand is 25-35 nucleotides in length and the second strand of the dsNA is 25-35 nucleotides in length, where the second strand is sufficiently complementary to a target EGFR cDNA sequence of Table 13 along at least 15 nucleotides of the second strand length to reduce EGFR target gene expression when the double stranded nucleic acid is introduced into a mammalian cell.

In one embodiment, the isolated dsNA possesses a duplex region of at least 25 base pairs.

Another aspect of the invention provides a method for treating or preventing an EGFR-associated disease or disorder in a subject involving administering an isolated dsNA of the invention and a pharmaceutically acceptable carrier to the subject in an amount sufficient to treat or prevent the EGFR-associated disease or disorder in the subject, thereby treating or preventing the EGFR-associated disease or disorder in the subject.

In one embodiment, the EGFR-associated disease or disorder is selected from the group consisting of squamous cell carcinoma of the head and neck (SCCHN), lung and colorectal cancer.

Another aspect of the invention provides an isolated double stranded nucleic acid (dsNA) possessing first and second nucleic acid strands, where the dsNA possesses blunt ends, where each of the first and second strands consists of the same number of nucleotide residues and is at most 35 nucleotides in length, where the second strand is sufficiently complementary to a target EGFR cDNA sequence of Table 13 along at least 15 nucleotides of the second strand length to reduce EGFR target gene expression when the double stranded nucleic acid is introduced into a mammalian cell, and where the dsNA reduces EGFR mRNA levels by at least 70% when assayed *in vitro* in a mammalian cell at an effective concentration in the environment of the cell of 1 nanomolar or less. In one embodiment, each of the first strand and the second strand is 25-35 nucleotides in length.

In one embodiment, each of the first and the second strands has a length which is 26-30 nucleotides. Optionally, each of the first and the second strands has a length which is 27 nucleotides.

Another aspect of the invention provides an isolated double stranded nucleic acid (dsNA) possessing first and second nucleic acid strands, where the dsNA possesses a blunt end, where each of the first and second strands consists of the same number of nucleotide residues and is at most 35 nucleotides in length, where the ultimate and penultimate residues of the 3' terminus of the first strand and the ultimate and penultimate residues of the 5' terminus of the second strand form one or two mismatched based pairs, where the second strand is sufficiently complementary to a target EGFR cDNA sequence selected from Table 13 along at least 15 nucleotides of the second strand length to reduce EGFR target gene expression when the double stranded nucleic acid is introduced into a mammalian cell, and where the dsNA reduces EGFR mRNA levels by at least 70% when assayed *in vitro* in a mammalian cell at an effective concentration in the environment of the cell of 1 nanomolar or less.

A further aspect of the invention provides a composition possessing EGFR inhibitory activity consisting essentially of an isolated double stranded ribonucleic acid (dsNA) possessing first and second nucleic acid strands, where the dsNA comprises a blunt end, where each of the first and second strands consists of the same number of nucleotide residues and is at most 35 nucleotides in length, where the ultimate and penultimate residues of the 3'

terminus of the first strand and the ultimate and penultimate residues of the 5' terminus of the second strand form one or two mismatched base pairs, where the second strand is sufficiently complementary to a target EGFR cDNA sequence of Table 13 along at least 15 nucleotides of the second strand length to reduce EGFR target gene expression when the double stranded nucleic acid is introduced into a mammalian cell, and where the dsNA reduces EGFR mRNA levels by at least 70% when assayed *in vitro* in a mammalian cell at an effective concentration in the environment of the cell of 1 nanomolar or less.

The present invention is also directed to compounds, compositions, and methods relating to traits, diseases and conditions that respond to the modulation of expression and/or activity of genes involved in EGFR gene expression pathways or other cellular processes that mediate the maintenance or development of such traits, diseases and conditions. In certain aspects, the invention relates to small nucleic acid molecules that are capable of being processed by the Dicer enzyme, such as Dicer substrate siRNAs (DsiRNAs) capable of mediating RNA interference (RNAi) against EGFR gene expression. The anti-EGFR dsNAs of the invention are useful, for example, in providing compositions for treatment of traits, diseases and conditions that can respond to modulation of EGFR in a subject, such as cancer and/or other proliferative diseases, disorders, or conditions. Efficacy, potency, toxicity and other effects of an anti-EGFR dsNA can be examined in one or more animal models of proliferative disease (exemplary animal models of proliferative disease are recited below).

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 shows the structures of exemplary DsiRNA agents of the invention targeting a site in the EGFR RNA referred to herein as the "EGFR-4249" target site. UPPER case = unmodified RNA, lower case = DNA, **Bold** = mismatch base pair nucleotides; arrowheads indicate projected Dicer enzyme cleavage sites; dashed line indicates sense strand (top strand) sequences corresponding to the projected Argonaute 2 (Ago2) cleavage site within the targeted EGFR sequence.

Figures 2A to 2D present primary screen data showing DsiRNA-mediated knockdown of human EGFR (Figures 2A and 2B) and mouse EGFR (Figures 2C and 2D) in human and mouse cells, respectively. For each DsiRNA tested, two independent qPCR amplicons were assayed (in human cells, amplicons "1068-1232" and "4704-4789" were assayed, while in mouse cells, amplicons "1955-2098" and "3602-3699" were assayed).

Figures 3A to 3D show histograms of human and mouse EGFR inhibitory efficacies observed for indicated DsiRNAs. "P1" indicates phase 1 (primary screen), while "P2" indicates phase 2. In phase 1, DsiRNAs were tested at 1 nM in the environment of HeLa cells (human cell assays; *Figures 3A and 3B*) or mouse cells (Hepa1-6 cell assays; *Figures 3C and 3D*). In phase 2, DsiRNAs were tested at 1 nM, at 0.3 nM and at 0.1 nM in the environment of human HeLa cells or mouse Hepa1-6 cells. Individual bars represent average human (*Figures 3A and 3B*) or mouse (*Figures 3C and 3D*) EGFR levels observed in triplicate, with standard errors shown. Human EGFR levels were normalized to HPRT and SFRS9 levels, while mouse EGFR levels were normalized to HPRT and Rpl23 levels.

Figures 4A to 4I present modification patterns employed (*Figure 4A*) and bar graphs showing efficacy data (*Figures 4B to 4I*) for six different 2'-O-methyl modification patterns ("M1", "M11", "M20", "M25", "M35", and "M8", respectively) each across 32 EGFR-targeting DsiRNAs in human HeLa cells at 0.1 nM, 0.3 nM and 1 nM.

DETAILED DESCRIPTION OF THE INVENTION

The present invention is directed to compositions that contain double stranded RNA ("dsRNA"), and methods for preparing them, that are capable of reducing the level and/or expression of the EGFR gene *in vivo* or *in vitro*. One of the strands of the dsRNA contains a region of nucleotide sequence that has a length that ranges from 19 to 35 nucleotides that can direct the destruction and/or translational inhibition of the targeted EGFR transcript.

Definitions

Unless defined otherwise, all technical and scientific terms used herein have the meaning commonly understood by a person skilled in the art to which this invention belongs. The following references provide one of skill with a general definition of many of the terms used in this invention: Singleton *et al.*, Dictionary of Microbiology and Molecular Biology (2nd ed. 1994); The Cambridge Dictionary of Science and Technology (Walker ed., 1988); The Glossary of Genetics, 5th Ed., R. Rieger et al. (eds.), Springer Verlag (1991); and Hale & Marham, The Harper Collins Dictionary of Biology (1991). As used herein, the following terms have the meanings ascribed to them below, unless specified otherwise.

The present invention features one or more DsiRNA molecules that can modulate (*e.g.*, inhibit) EGFR expression. The DsiRNAs of the invention optionally can be used in combination with modulators of other genes and/or gene products associated with the

maintenance or development of diseases or disorders associated with EGFR misregulation (*e.g.*, tumor formation and/or growth, etc.). The DsiRNA agents of the invention modulate EGFR RNAs such as those corresponding to the cDNA sequences referred to by GenBank Accession Nos. NM_005228.3 (human EGFR) and NM_207655.2 (mouse EGFR), which are recited below and referred to herein generally as “EGFR.”

The below description of the various aspects and embodiments of the invention is provided with reference to exemplary EGFR RNAs, generally referred to herein as EGFR. However, such reference is meant to be exemplary only and the various aspects and embodiments of the invention are also directed to alternate EGFR RNAs, such as mutant EGFR RNAs or additional EGFR splice variants. Certain aspects and embodiments are also directed to other genes involved in EGFR pathways, including genes whose misregulation acts in association with that of EGFR (or is affected or affects EGFR regulation) to produce phenotypic effects that may be targeted for treatment (*e.g.*, tumor formation and/or growth, etc.). (The EGFR pathway, MAPK, Akt, JNK and MET pathways are examples of pathways for which misregulation of genes can act in association with that of EGFR.) Such additional genes can be targeted using dsRNA and the methods described herein for use of EGFR targeting dsRNAs. Thus, the inhibition and the effects of such inhibition of the other genes can be performed as described herein.

The term “EGFR” refers to nucleic acid sequences encoding an EGFR protein, peptide, or polypeptide (*e.g.*, EGFR transcripts, such as the sequences of EGFR Genbank Accession Nos. NM_005228.3 and NM_207655.2). In certain embodiments, the term “EGFR” is also meant to include other EGFR encoding sequence, such as other EGFR isoforms, mutant EGFR genes, splice variants of EGFR genes, and EGFR gene polymorphisms. The term “EGFR” is also used to refer to the polypeptide gene product of an EGFR gene/transcript, *e.g.*, an EGFR protein, peptide, or polypeptide, such as those encoded by EGFR Genbank Accession Nos. NM_005228.3 and NM_207655.2.

As used herein, a “EGFR-associated disease or disorder” refers to a disease or disorder known in the art to be associated with altered EGFR expression, level and/or activity. Notably, an “EGFR-associated disease or disorder” includes cancer and/or proliferative diseases, conditions, or disorders. Exemplary “EGFR-associated disease or disorders” include colorectal, lung (*e.g.*, NSCLC), squamous cell carcinoma (*e.g.*, of the head and neck (SCCHN)), bladder, brain, breast, cervical (uterine), endometrial (uterine),

esophageal, liver, oropharyngeal, ovarian, pancreatic, renal, skin (melanoma) and stomach (GIST) cancers.

By "proliferative disease" or "cancer" as used herein is meant a disease, condition, trait, genotype or phenotype characterized by unregulated cell growth or replication as is known in the art; including squamous cell carcinoma (e.g., of the head and neck (SCCHN)), colorectal cancer, lung cancer, leukemias, for example, acute myelogenous leukemia (AML), chronic myelogenous leukemia (CML), acute lymphocytic leukemia (ALL), and chronic lymphocytic leukemia, AIDS related cancers such as Kaposi's sarcoma; breast cancers; bone cancers such as Osteosarcoma, Chondrosarcomas, Ewing's sarcoma, Fibrosarcomas, Giant cell tumors, Adamantinomas, and Chordomas; Brain cancers such as Meningiomas, Glioblastomas, Lower-Grade Astrocytomas, Oligodendrocytomas, Pituitary Tumors, Schwannomas, and Metastatic brain cancers; cancers of the head and neck including various lymphomas such as mantle cell lymphoma, non-Hodgkins lymphoma, adenoma, laryngeal carcinoma, gallbladder and bile duct cancers, cancers of the retina such as retinoblastoma, cancers of the esophagus, gastric cancers, multiple myeloma, ovarian cancer, uterine cancer, thyroid cancer, testicular cancer, endometrial cancer, melanoma, bladder cancer, prostate cancer, lung cancer (including non-small cell lung carcinoma), pancreatic cancer, sarcomas, Wilms' tumor, cervical cancer, head and neck cancer, skin cancers, nasopharyngeal carcinoma, liposarcoma, epithelial carcinoma, renal cell carcinoma, gallbladder adenocarcinoma, parotid adenocarcinoma, endometrial sarcoma, multidrug resistant cancers; and proliferative diseases and conditions, such as neovascularization associated with tumor angiogenesis, macular degeneration (*e.g.*, wet/dry AMD), corneal neovascularization, diabetic retinopathy, neovascular glaucoma, myopic degeneration and other proliferative diseases and conditions such as restenosis and polycystic kidney disease, and other cancer or proliferative disease, condition, trait, genotype or phenotype that can respond to the modulation of disease related gene expression in a cell or tissue, alone or in combination with other therapies.

In certain embodiments, dsRNA-mediated inhibition of an EGFR target sequence is assessed. In such embodiments, EGFR RNA levels can be assessed by art-recognized methods (*e.g.*, RT-PCR, Northern blot, expression array, etc.), optionally *via* comparison of EGFR levels in the presence of an anti-EGFR dsRNA of the invention relative to the absence of such an anti-EGFR dsRNA. In certain embodiments, EGFR levels in the presence of an anti-EGFR dsRNA are compared to those observed in the presence of vehicle alone, in the

presence of a dsRNA directed against an unrelated target RNA, or in the absence of any treatment.

It is also recognized that levels of EGFR protein can be assessed and that EGFR protein levels are, under different conditions, either directly or indirectly related to EGFR RNA levels and/or the extent to which a dsRNA inhibits EGFR expression, thus art-recognized methods of assessing EGFR protein levels (*e.g.*, Western blot, immunoprecipitation, other antibody-based methods, etc.) can also be employed to examine the inhibitory effect of a dsRNA of the invention.

An anti-EGFR dsRNA of the invention is deemed to possess “EGFR inhibitory activity” if a statistically significant reduction in EGFR RNA (or when the EGFR protein is assessed, EGFR protein levels) is seen when an anti-EGFR dsRNA of the invention is administered to a system (*e.g.*, cell-free *in vitro* system), cell, tissue or organism, as compared to a selected control. The distribution of experimental values and the number of replicate assays performed will tend to dictate the parameters of what levels of reduction in EGFR RNA (either as a % or in absolute terms) is deemed statistically significant (as assessed by standard methods of determining statistical significance known in the art). However, in certain embodiments, “EGFR inhibitory activity” is defined based upon a % or absolute level of reduction in the level of EGFR in a system, cell, tissue or organism. For example, in certain embodiments, a dsRNA of the invention is deemed to possess EGFR inhibitory activity if at least a 5% reduction or at least a 10% reduction in EGFR RNA is observed in the presence of a dsRNA of the invention relative to EGFR levels seen for a suitable control. (For example, *in vivo* EGFR levels in a tissue and/or subject can, in certain embodiments, be deemed to be inhibited by a dsRNA agent of the invention if, *e.g.*, a 5% or 10% reduction in EGFR levels is observed relative to a control.) In certain other embodiments, a dsRNA of the invention is deemed to possess EGFR inhibitory activity if EGFR RNA levels are observed to be reduced by at least 15% relative to a selected control, by at least 20% relative to a selected control, by at least 25% relative to a selected control, by at least 30% relative to a selected control, by at least 35% relative to a selected control, by at least 40% relative to a selected control, by at least 45% relative to a selected control, by at least 50% relative to a selected control, by at least 55% relative to a selected control, by at least 60% relative to a selected control, by at least 65% relative to a selected control, by at least 70% relative to a selected control, by at least 75% relative to a selected control, by at least 80% relative to a selected control, by at least 85% relative to a selected control, by at least 90% relative to a selected

control, by at least 95% relative to a selected control, by at least 96% relative to a selected control, by at least 97% relative to a selected control, by at least 98% relative to a selected control or by at least 99% relative to a selected control. In some embodiments, complete inhibition of EGFR is required for a dsRNA to be deemed to possess EGFR inhibitory activity. In certain models (*e.g.*, cell culture), a dsRNA is deemed to possess EGFR inhibitory activity if at least a 50% reduction in EGFR levels is observed relative to a suitable control. In certain other embodiments, a dsRNA is deemed to possess EGFR inhibitory activity if at least an 80% reduction in EGFR levels is observed relative to a suitable control.

By way of specific example, in Example 2 below, a series of DsiRNAs targeting EGFR were tested for the ability to reduce EGFR mRNA levels in human HeLa or mouse Hepa 1-6 cells *in vitro*, at 1 nM concentrations in the environment of such cells and in the presence of a transfection agent (Lipofectamine™ RNAiMAX, Invitrogen). Within Example 2 below, EGFR inhibitory activity was initially ascribed to those DsiRNAs that were observed to effect at least a 70% reduction of EGFR mRNA levels under the assayed conditions. It is contemplated that EGFR inhibitory activity could also be attributed to a dsRNA under either more or less stringent conditions than those employed for Example 2 below, even when the same or a similar assay and conditions are employed. For example, in certain embodiments, a tested dsRNA of the invention is deemed to possess EGFR inhibitory activity if at least a 10% reduction, at least a 20% reduction, at least a 30% reduction, at least a 40% reduction, at least a 50% reduction, at least a 60% reduction, at least a 75% reduction, at least an 80% reduction, at least an 85% reduction, at least a 90% reduction, or at least a 95% reduction in EGFR mRNA levels is observed in a mammalian cell line *in vitro* at 1 nM dsRNA concentration or lower in the environment of a cell, relative to a suitable control.

Use of other endpoints for determination of whether a double stranded RNA of the invention possesses EGFR inhibitory activity is also contemplated. Specifically, in one embodiment, in addition to or as an alternative to assessing EGFR mRNA levels, the ability of a tested dsRNA to reduce EGFR protein levels (*e.g.*, at 48 hours after contacting a mammalian cell *in vitro* or *in vivo*) is assessed, and a tested dsRNA is deemed to possess EGFR inhibitory activity if at least a 10% reduction, at least a 20% reduction, at least a 30% reduction, at least a 40% reduction, at least a 50% reduction, at least a 60% reduction, at least a 70% reduction, at least a 75% reduction, at least an 80% reduction, at least an 85% reduction, at least a 90% reduction, or at least a 95% reduction in EGFR protein levels is observed in a mammalian cell contacted with the assayed double stranded RNA *in vitro* or *in*

vivo, relative to a suitable control. Additional endpoints contemplated include, *e.g.*, assessment of a phenotype associated with reduction of EGFR levels – *e.g.*, reduction of growth of a contacted mammalian cell line *in vitro* and/or reduction of growth of a tumor *in vivo*, including, *e.g.*, halting or reducing the growth of tumor or cancer cell levels as described in greater detail elsewhere herein.

EGFR inhibitory activity can also be evaluated over time (duration) and over concentration ranges (potency), with assessment of what constitutes a dsRNA possessing EGFR inhibitory activity adjusted in accordance with concentrations administered and duration of time following administration. Thus, in certain embodiments, a dsRNA of the invention is deemed to possess EGFR inhibitory activity if at least a 50% reduction in EGFR activity is observed/persists at a duration of time of 2 hours, 5 hours, 10 hours, 1 day, 2 days, 3 days, 4 days, 5 days, 6 days, 7 days, 8 days, 9 days, 10 days or more after administration of the dsRNA to a cell or organism. In additional embodiments, a dsRNA of the invention is deemed to be a potent EGFR inhibitory agent if EGFR inhibitory activity (*e.g.*, in certain embodiments, at least 50% inhibition of EGFR) is observed at a concentration of 1 nM or less, 500 pM or less, 200 pM or less, 100 pM or less, 50 pM or less, 20 pM or less, 10 pM or less, 5 pM or less, 2 pM or less or even 1 pM or less in the environment of a cell, for example, within an *in vitro* assay for EGFR inhibitory activity as described herein. In certain embodiments, a potent EGFR inhibitory dsRNA of the invention is defined as one that is capable of EGFR inhibitory activity (*e.g.*, in certain embodiments, at least 20% reduction of EGFR levels) at a formulated concentration of 10 mg/kg or less when administered to a subject in an effective delivery vehicle (*e.g.*, an effective lipid nanoparticle formulation). Preferably, a potent EGFR inhibitory dsRNA of the invention is defined as one that is capable of EGFR inhibitory activity (*e.g.*, in certain embodiments, at least 50% reduction of EGFR levels) at a formulated concentration of 5 mg/kg or less when administered to a subject in an effective delivery vehicle. More preferably, a potent EGFR inhibitory dsRNA of the invention is defined as one that is capable of EGFR inhibitory activity (*e.g.*, in certain embodiments, at least 50% reduction of EGFR levels) at a formulated concentration of 5 mg/kg or less when administered to a subject in an effective delivery vehicle. Optionally, a potent EGFR inhibitory dsRNA of the invention is defined as one that is capable of EGFR inhibitory activity (*e.g.*, in certain embodiments, at least 50% reduction of EGFR levels) at a formulated concentration of 2 mg/kg or less, or even 1 mg/kg or less, when administered to a subject in an effective delivery vehicle.

In certain embodiments, potency of a dsRNA of the invention is determined in reference to the number of copies of a dsRNA present in the cytoplasm of a target cell that are required to achieve a certain level of target gene knockdown. For example, in certain embodiments, a potent dsRNA is one capable of causing 50% or greater knockdown of a target mRNA when present in the cytoplasm of a target cell at a copy number of 1000 or fewer RISC-loaded antisense strands per cell. More preferably, a potent dsRNA is one capable of producing 50% or greater knockdown of a target mRNA when present in the cytoplasm of a target cell at a copy number of 500 or fewer RISC-loaded antisense strands per cell. Optionally, a potent dsRNA is one capable of producing 50% or greater knockdown of a target mRNA when present in the cytoplasm of a target cell at a copy number of 300 or fewer RISC-loaded antisense strands per cell.

In further embodiments, the potency of a DsiRNA of the invention can be defined in reference to a 19 to 23mer dsRNA directed to the same target sequence within the same target gene. For example, a DsiRNA of the invention that possesses enhanced potency relative to a corresponding 19 to 23mer dsRNA can be a DsiRNA that reduces a target gene by an additional 5% or more, an additional 10% or more, an additional 20% or more, an additional 30% or more, an additional 40% or more, or an additional 50% or more as compared to a corresponding 19 to 23mer dsRNA, when assayed in an in vitro assay as described herein at a sufficiently low concentration to allow for detection of a potency difference (e.g., transfection concentrations at or below 1 nM in the environment of a cell, at or below 100 pM in the environment of a cell, at or below 10 pM in the environment of a cell, at or below 1 nM in the environment of a cell, in an in vitro assay as described herein; notably, it is recognized that potency differences can be best detected via performance of such assays across a range of concentrations – e.g., 0.1 pM to 10 nM – for purpose of generating a dose-response curve and identifying an IC₅₀ value associated with a DsiRNA/dsRNA).

EGFR inhibitory levels and/or EGFR levels may also be assessed indirectly, e.g., measurement of a reduction of the size, number and/or rate of growth or spread of polyps or tumors in a subject may be used to assess EGFR levels and/or EGFR inhibitory efficacy of a double-stranded nucleic acid of the instant invention.

In certain embodiments, the phrase “consists essentially of” is used in reference to the anti-EGFR dsRNAs of the invention. In some such embodiments, “consists essentially of” refers to a composition that comprises a dsRNA of the invention which possesses at least a certain level of EGFR inhibitory activity (e.g., at least 50% EGFR inhibitory activity) and

that also comprises one or more additional components and/or modifications that do not significantly impact the EGFR inhibitory activity of the dsRNA. For example, in certain embodiments, a composition “consists essentially of” a dsRNA of the invention where modifications of the dsRNA of the invention and/or dsRNA-associated components of the composition do not alter the EGFR inhibitory activity (optionally including potency or duration of EGFR inhibitory activity) by greater than 3%, greater than 5%, greater than 10%, greater than 15%, greater than 20%, greater than 25%, greater than 30%, greater than 35%, greater than 40%, greater than 45%, or greater than 50% relative to the dsRNA of the invention in isolation. In certain embodiments, a composition is deemed to consist essentially of a dsRNA of the invention even if more dramatic reduction of EGFR inhibitory activity (*e.g.*, 80% reduction, 90% reduction, etc. in efficacy, duration and/or potency) occurs in the presence of additional components or modifications, yet where EGFR inhibitory activity is not significantly elevated (*e.g.*, observed levels of EGFR inhibitory activity are within 10% those observed for the isolated dsRNA of the invention) in the presence of additional components and/or modifications.

As used herein, the phrase “dsRNA reduces EGFR mRNA levels by at least X% when assayed *in vitro* in a mammalian cell at an effective concentration in the environment of said cell of 1 nanomolar or less” refers to a requirement for the dsRNA to reduce the native EGFR mRNA levels of a HeLa cell population by at least X%, when assayed at a transfection concentration of 1 nanomolar or less in the presence of Lipofectamine™ RNAiMAX (Invitrogen) and following manufacturer’s instructions. Such HeLa cells are obtained from ATCC and maintained in DMEM (HyClone) supplemented with 10% fetal bovine serum (HyClone) at 37°C under 5% CO₂. EGFR mRNA levels are then assayed at 24h or 48h post-transfection to assess % inhibition, with respect to an appropriate control as described elsewhere herein.

As used herein, the term “nucleic acid” refers to deoxyribonucleotides, ribonucleotides, or modified nucleotides, and polymers thereof in single- or double-stranded form. The term encompasses nucleic acids containing known nucleotide analogs or modified backbone residues or linkages, which are synthetic, naturally occurring, and non-naturally occurring, which have similar binding properties as the reference nucleic acid, and which are metabolized in a manner similar to the reference nucleotides. Examples of such analogs include, without limitation, phosphorothioates, phosphoramidates, methyl phosphonates,

chiral-methyl phosphonates, 2-O-methyl ribonucleotides, peptide-nucleic acids (PNAs) and unlocked nucleic acids (UNAs; see, *e.g.*, Jensen *et al. Nucleic Acids Symposium Series 52*: 133-4), and derivatives thereof.

As used herein, "nucleotide" is used as recognized in the art to include those with natural bases (standard), and modified bases well known in the art. Such bases are generally located at the 1' position of a nucleotide sugar moiety. Nucleotides generally comprise a base, sugar and a phosphate group. The nucleotides can be unmodified or modified at the sugar, phosphate and/or base moiety, (also referred to interchangeably as nucleotide analogs, modified nucleotides, non-natural nucleotides, non-standard nucleotides and other; see, *e.g.*, Usman and McSwiggen, *supra*; Eckstein, *et al.*, International PCT Publication No. WO 92/07065; Usman *et al.*, International PCT Publication No. WO 93/15187; Uhlman & Peyman, *supra*, all are hereby incorporated by reference herein). There are several examples of modified nucleic acid bases known in the art as summarized by Limbach, *et al. Nucleic Acids Res.* 22:2183, 1994. Some of the non-limiting examples of base modifications that can be introduced into nucleic acid molecules include, hypoxanthine, purine, pyridin-4-one, pyridin-2-one, phenyl, pseudouracil, 2,4,6-trimethoxy benzene, 3-methyl uracil, dihydrouridine, naphthyl, aminophenyl, 5-alkylcytidines (*e.g.*, 5-methylcytidine), 5-alkyluridines (*e.g.*, ribothymidine), 5-halouridine (*e.g.*, 5-bromouridine) or 6-azapyrimidines or 6-alkylpyrimidines (*e.g.* 6-methyluridine), propyne, and others (Burgin, *et al.*, *Biochemistry* 35:14090, 1996; Uhlman & Peyman, *supra*). By "modified bases" in this aspect is meant nucleotide bases other than adenine, guanine, cytosine and uracil at 1' position or their equivalents.

As used herein, "modified nucleotide" refers to a nucleotide that has one or more modifications to the nucleoside, the nucleobase, pentose ring, or phosphate group. For example, modified nucleotides exclude ribonucleotides containing adenosine monophosphate, guanosine monophosphate, uridine monophosphate, and cytidine monophosphate and deoxyribonucleotides containing deoxyadenosine monophosphate, deoxyguanosine monophosphate, deoxythymidine monophosphate, and deoxycytidine monophosphate. Modifications include those naturally occurring that result from modification by enzymes that modify nucleotides, such as methyltransferases. Modified nucleotides also include synthetic or non-naturally occurring nucleotides. Synthetic or non-naturally occurring modifications in nucleotides include those with 2' modifications, *e.g.*, 2'-methoxyethoxy, 2'-fluoro, 2'-allyl, 2'-O-[2-(methylamino)-2-oxoethyl], 4'-thio, 4'-CH₂-O-2'-

bridge, 4'-(CH₂)₂-O-2'-bridge, 2'-LNA or other bicyclic or "bridged" nucleoside analog, and 2'-O-(N-methylcarbamate) or those comprising base analogs. In connection with 2'-modified nucleotides as described for the present disclosure, by "amino" is meant 2'-NH₂ or 2'-O-NH₂, which can be modified or unmodified. Such modified groups are described, *e.g.*, in Eckstein *et al.*, U.S. Pat. No. 5,672,695 and Matulic-Adamic *et al.*, U.S. Pat. No. 6,248,878.

"Modified nucleotides" of the instant invention can also include nucleotide analogs as described above.

In reference to the nucleic acid molecules of the present disclosure, modifications may exist upon these agents in patterns on one or both strands of the double stranded ribonucleic acid (dsRNA). As used herein, "alternating positions" refers to a pattern where every other nucleotide is a modified nucleotide or there is an unmodified nucleotide (*e.g.*, an unmodified ribonucleotide) between every modified nucleotide over a defined length of a strand of the dsRNA (*e.g.*, 5'-MNMNMN-3'; 3'-MNMNMN-5'; where M is a modified nucleotide and N is an unmodified nucleotide). The modification pattern starts from the first nucleotide position at either the 5' or 3' terminus according to a position numbering convention, *e.g.*, as described herein (in certain embodiments, position 1 is designated in reference to the terminal residue of a strand following a projected Dicer cleavage event of a DsiRNA agent of the invention; thus, position 1 does not always constitute a 3' terminal or 5' terminal residue of a pre-processed agent of the invention). The pattern of modified nucleotides at alternating positions may run the full length of the strand, but in certain embodiments includes at least 4, 6, 8, 10, 12, 14 nucleotides containing at least 2, 3, 4, 5, 6 or 7 modified nucleotides, respectively. As used herein, "alternating pairs of positions" refers to a pattern where two consecutive modified nucleotides are separated by two consecutive unmodified nucleotides over a defined length of a strand of the dsRNA (*e.g.*, 5'-MMNNMMNNMMNN-3'; 3'-MMNNMMNNMMNN-5'; where M is a modified nucleotide and N is an unmodified nucleotide). The modification pattern starts from the first nucleotide position at either the 5' or 3' terminus according to a position numbering convention such as those described herein. The pattern of modified nucleotides at alternating positions may run the full length of the strand, but preferably includes at least 8, 12, 16, 20, 24, 28 nucleotides containing at least 4, 6, 8, 10, 12 or 14 modified nucleotides, respectively. It is emphasized that the above modification patterns are exemplary and are not intended as limitations on the scope of the invention.

As used herein, "base analog" refers to a heterocyclic moiety which is located at the 1'

position of a nucleotide sugar moiety in a modified nucleotide that can be incorporated into a nucleic acid duplex (or the equivalent position in a nucleotide sugar moiety substitution that can be incorporated into a nucleic acid duplex). In the dsRNAs of the invention, a base analog is generally either a purine or pyrimidine base excluding the common bases guanine (G), cytosine (C), adenine (A), thymine (T), and uracil (U). Base analogs can duplex with other bases or base analogs in dsRNAs. Base analogs include those useful in the compounds and methods of the invention., e.g., those disclosed in US Pat. Nos. 5,432,272 and 6,001,983 to Benner and US Patent Publication No. 20080213891 to Manoharan, which are herein incorporated by reference. Non-limiting examples of bases include hypoxanthine (I), xanthine (X), 3 β -D-ribofuranosyl-(2,6-diaminopyrimidine) (K), 3- β -D-ribofuranosyl-(1-methyl-pyrazolo[4,3-d]pyrimidine-5,7(4H,6H)-dione) (P), iso-cytosine (iso-C), iso-guanine (iso-G), 1- β -D-ribofuranosyl-(5-nitroindole), 1- β -D-ribofuranosyl-(3-nitropyrrole), 5-bromouracil, 2-aminopurine, 4-thio-dT, 7-(2-thienyl)-imidazo[4,5-b]pyridine (Ds) and pyrrole-2-carbaldehyde (Pa), 2-amino-6-(2-thienyl)purine (S), 2-oxopyridine (Y), difluorotolyl, 4-fluoro-6-methylbenzimidazole, 4-methylbenzimidazole, 3-methyl isocarbostyryl, 5-methyl isocarbostyryl, and 3-methyl-7-propynyl isocarbostyryl, 7-azaindolyl, 6-methyl-7-azaindolyl, imidizopyridinyl, 9-methyl-imidizopyridinyl, pyrrolopyrizinyl, isocarbostyryl, 7-propynyl isocarbostyryl, propynyl-7-azaindolyl, 2,4,5-trimethylphenyl, 4-methylindolyl, 4,6-dimethylindolyl, phenyl, naphthalenyl, anthracenyl, phenanthracenyl, pyrenyl, stilbenzyl, tetracenyl, pentacenyl, and structural derivatives thereof (Schweitzer et al., J. Org. Chem., 59:7238-7242 (1994); Berger et al., Nucleic Acids Research, 28(15):2911-2914 (2000); Moran et al., J. Am. Chem. Soc., 119:2056-2057 (1997); Morales et al., J. Am. Chem. Soc., 121:2323-2324 (1999); Guckian et al., J. Am. Chem. Soc., 118:8182-8183 (1996); Morales et al., J. Am. Chem. Soc., 122(6):1001-1007 (2000); McMinn et al., J. Am. Chem. Soc., 121:11585-11586 (1999); Guckian et al., J. Org. Chem., 63:9652-9656 (1998); Moran et al., Proc. Natl. Acad. Sci., 94:10506-10511 (1997); Das et al., J. Chem. Soc., Perkin Trans., 1:197-206 (2002); Shibata et al., J. Chem. Soc., Perkin Trans., 1: 1605-1611 (2001); Wu et al., J. Am. Chem. Soc., 122(32):7621-7632 (2000); O'Neill et al., J. Org. Chem., 67:5869-5875 (2002); Chaudhuri et al., J. Am. Chem. Soc., 117:10434-10442 (1995); and U.S. Pat. No. 6,218,108.). Base analogs may also be a universal base.

As used herein, "universal base" refers to a heterocyclic moiety located at the 1' position of a nucleotide sugar moiety in a modified nucleotide, or the equivalent position in a

nucleotide sugar moiety substitution, that, when present in a nucleic acid duplex, can be positioned opposite more than one type of base without altering the double helical structure (e.g., the structure of the phosphate backbone). Additionally, the universal base does not destroy the ability of the single stranded nucleic acid in which it resides to duplex to a target nucleic acid. The ability of a single stranded nucleic acid containing a universal base to duplex a target nucleic acid can be assayed by methods apparent to one in the art (e.g., UV absorbance, circular dichroism, gel shift, single stranded nuclease sensitivity, etc.). Additionally, conditions under which duplex formation is observed may be varied to determine duplex stability or formation, e.g., temperature, as melting temperature (T_m) correlates with the stability of nucleic acid duplexes. Compared to a reference single stranded nucleic acid that is exactly complementary to a target nucleic acid, the single stranded nucleic acid containing a universal base forms a duplex with the target nucleic acid that has a lower T_m than a duplex formed with the complementary nucleic acid. However, compared to a reference single stranded nucleic acid in which the universal base has been replaced with a base to generate a single mismatch, the single stranded nucleic acid containing the universal base forms a duplex with the target nucleic acid that has a higher T_m than a duplex formed with the nucleic acid having the mismatched base.

Some universal bases are capable of base pairing by forming hydrogen bonds between the universal base and all of the bases guanine (G), cytosine (C), adenine (A), thymine (T), and uracil (U) under base pair forming conditions. A universal base is not a base that forms a base pair with only one single complementary base. In a duplex, a universal base may form no hydrogen bonds, one hydrogen bond, or more than one hydrogen bond with each of G, C, A, T, and U opposite to it on the opposite strand of a duplex. Preferably, the universal bases does not interact with the base opposite to it on the opposite strand of a duplex. In a duplex, base pairing between a universal base occurs without altering the double helical structure of the phosphate backbone. A universal base may also interact with bases in adjacent nucleotides on the same nucleic acid strand by stacking interactions. Such stacking interactions stabilize the duplex, especially in situations where the universal base does not form any hydrogen bonds with the base positioned opposite to it on the opposite strand of the duplex. Non-limiting examples of universal-binding nucleotides include inosine, 1- β -D-ribofuranosyl-5-nitroindole, and/or 1- β -D-ribofuranosyl-3-nitropyrrole (US Pat. Appl. Publ. No. 20070254362 to Quay et al.; Van Aerschot et al., An acyclic 5-nitroindazole nucleoside analogue as ambiguous nucleoside. *Nucleic Acids Res.* 1995 Nov 11;23(21):4363-70;

Loakes et al., 3-Nitropyrrole and 5-nitroindole as universal bases in primers for DNA sequencing and PCR. *Nucleic Acids Res.* 1995 Jul 11;23(13):2361-6; Loakes and Brown, 5-Nitroindole as an universal base analogue. *Nucleic Acids Res.* 1994 Oct 11;22(20):4039-43).

As used herein, “loop” refers to a structure formed by a single strand of a nucleic acid, in which complementary regions that flank a particular single stranded nucleotide region hybridize in a way that the single stranded nucleotide region between the complementary regions is excluded from duplex formation or Watson-Crick base pairing. A loop is a single stranded nucleotide region of any length. Examples of loops include the unpaired nucleotides present in such structures as hairpins, stem loops, or extended loops.

As used herein, “extended loop” in the context of a dsRNA refers to a single stranded loop and in addition 1, 2, 3, 4, 5, 6 or up to 20 base pairs or duplexes flanking the loop. In an extended loop, nucleotides that flank the loop on the 5’ side form a duplex with nucleotides that flank the loop on the 3’ side. An extended loop may form a hairpin or stem loop.

As used herein, “tetraloop” in the context of a dsRNA refers to a loop (a single stranded region) consisting of four nucleotides that forms a stable secondary structure that contributes to the stability of an adjacent Watson-Crick hybridized nucleotides. Without being limited to theory, a tetraloop may stabilize an adjacent Watson-Crick base pair by stacking interactions. In addition, interactions among the four nucleotides in a tetraloop include but are not limited to non-Watson-Crick base pairing, stacking interactions, hydrogen bonding, and contact interactions (Cheong *et al.*, *Nature* 1990 Aug 16; 346(6285): 680-2; Heus and Pardi, *Science* 1991 Jul 12; 253(5016): 191-4). A tetraloop confers an increase in the melting temperature (T_m) of an adjacent duplex that is higher than expected from a simple model loop sequence consisting of four random bases. For example, a tetraloop can confer a melting temperature of at least 55°C in 10mM NaHPO₄ to a hairpin comprising a duplex of at least 2 base pairs in length. A tetraloop may contain ribonucleotides, deoxyribonucleotides, modified nucleotides, and combinations thereof. Examples of RNA tetraloops include the UNCG family of tetraloops (e.g., UUCG), the GNRA family of tetraloops (e.g., GAAA), and the CUUG tetraloop. (Woese et al., *Proc Natl Acad Sci U S A.* 1990 Nov;87(21):8467-71; Antao et al., *Nucleic Acids Res.* 1991 Nov 11;19(21):5901-5). Examples of DNA tetraloops include the d(GNNA) family of tetraloops (e.g., d(GTTA), the d(GNRA)) family of tetraloops, the d(GNAB) family of tetraloops, the d(CNNG) family of tetraloops, the d(TNCG) family of tetraloops (e.g., d(TTCG)). (Nakano et al. *Biochemistry*, 41 (48), 14281 -14292, 2002.; SHINJI et al. *Nippon Kagakkai Koen Yokoshu VOL.78th*;

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As used herein, the term “siRNA” refers to a double stranded nucleic acid in which each strand comprises RNA, RNA analog(s) or RNA and DNA. The siRNA comprises between 19 and 23 nucleotides or comprises 21 nucleotides. The siRNA typically has 2 bp overhangs on the 3' ends of each strand such that the duplex region in the siRNA comprises 17-21 nucleotides, or 19 nucleotides. Typically, the antisense strand of the siRNA is sufficiently complementary with the target sequence of the EGFR gene/RNA.

An anti-EGFR DsiRNA of the instant invention possesses strand lengths of at least 25 nucleotides. Accordingly, in certain embodiments, an anti-EGFR DsiRNA contains one oligonucleotide sequence, a first sequence, that is at least 25 nucleotides in length and no longer than 35 or up to 50 or more nucleotides. This sequence of RNA can be between 26 and 35, 26 and 34, 26 and 33, 26 and 32, 26 and 31, 26 and 30, and 26 and 29 nucleotides in length. This sequence can be 27 or 28 nucleotides in length or 27 nucleotides in length. The second sequence of the DsiRNA agent can be a sequence that anneals to the first sequence under biological conditions, such as within the cytoplasm of a eukaryotic cell. Generally, the second oligonucleotide sequence will have at least 19 complementary base pairs with the first oligonucleotide sequence, more typically the second oligonucleotide sequence will have 21 or more complementary base pairs, or 25 or more complementary base pairs with the first oligonucleotide sequence. In one embodiment, the second sequence is the same length as the first sequence, and the DsiRNA agent is blunt ended. In another embodiment, the ends of the DsiRNA agent have one or more overhangs.

In certain embodiments, the first and second oligonucleotide sequences of the DsiRNA agent exist on separate oligonucleotide strands that can be and typically are chemically synthesized. In some embodiments, both strands are between 26 and 35 nucleotides in length. In other embodiments, both strands are between 25 and 30 or 26 and 30 nucleotides in length. In one embodiment, both strands are 27 nucleotides in length, are completely complementary and have blunt ends. In certain embodiments of the instant invention, the first and second sequences of an anti-EGFR DsiRNA exist on separate RNA oligonucleotides (strands). In one embodiment, one or both oligonucleotide strands are capable of serving as a substrate for Dicer. In other embodiments, at least one modification is present that promotes Dicer to bind to the double-stranded RNA structure in an orientation that maximizes the double-stranded RNA structure's effectiveness in inhibiting gene expression. In certain embodiments of the instant invention, the anti-EGFR DsiRNA agent is

comprised of two oligonucleotide strands of differing lengths, with the anti-EGFR DsiRNA possessing a blunt end at the 3' terminus of a first strand (sense strand) and a 3' overhang at the 3' terminus of a second strand (antisense strand). The DsiRNA can also contain one or more deoxyribonucleic acid (DNA) base substitutions.

Suitable DsiRNA compositions that contain two separate oligonucleotides can be chemically linked outside their annealing region by chemical linking groups. Many suitable chemical linking groups are known in the art and can be used. Suitable groups will not block Dicer activity on the DsiRNA and will not interfere with the directed destruction of the RNA transcribed from the target gene. Alternatively, the two separate oligonucleotides can be linked by a third oligonucleotide such that a hairpin structure is produced upon annealing of the two oligonucleotides making up the DsiRNA composition. The hairpin structure will not block Dicer activity on the DsiRNA and will not interfere with the directed destruction of the target RNA.

As used herein, a dsRNA, *e.g.*, DsiRNA or siRNA, having a sequence "sufficiently complementary" to a target RNA or cDNA sequence (*e.g.*, EGFR mRNA) means that the dsRNA has a sequence sufficient to trigger the destruction of the target RNA (where a cDNA sequence is recited, the RNA sequence corresponding to the recited cDNA sequence) by the RNAi machinery (*e.g.*, the RISC complex) or process. For example, a dsRNA that is "sufficiently complementary" to a target RNA or cDNA sequence to trigger the destruction of the target RNA by the RNAi machinery or process can be identified as a dsRNA that causes a detectable reduction in the level of the target RNA in an appropriate assay of dsRNA activity (*e.g.*, an *in vitro* assay as described in Example 2 below), or, in further examples, a dsRNA that is sufficiently complementary to a target RNA or cDNA sequence to trigger the destruction of the target RNA by the RNAi machinery or process can be identified as a dsRNA that produces at least a 5%, at least a 10%, at least a 15%, at least a 20%, at least a 25%, at least a 30%, at least a 35%, at least a 40%, at least a 45%, at least a 50%, at least a 55%, at least a 60%, at least a 65%, at least a 70%, at least a 75%, at least a 80%, at least a 85%, at least a 90%, at least a 95%, at least a 98% or at least a 99% reduction in the level of the target RNA in an appropriate assay of dsRNA activity. In additional examples, a dsRNA that is sufficiently complementary to a target RNA or cDNA sequence to trigger the destruction of the target RNA by the RNAi machinery or process can be identified based upon assessment of the duration of a certain level of inhibitory activity with respect to the target RNA or protein levels in a cell or organism. For example, a dsRNA that is sufficiently

complementary to a target RNA or cDNA sequence to trigger the destruction of the target RNA by the RNAi machinery or process can be identified as a dsRNA capable of reducing target mRNA levels by at least 20% at least 48 hours post-administration of said dsRNA to a cell or organism. Preferably, a dsRNA that is sufficiently complementary to a target RNA or cDNA sequence to trigger the destruction of the target RNA by the RNAi machinery or process is identified as a dsRNA capable of reducing target mRNA levels by at least 40% at least 72 hours post-administration of said dsRNA to a cell or organism, by at least 40% at least four, five or seven days post-administration of said dsRNA to a cell or organism, by at least 50% at least 48 hours post-administration of said dsRNA to a cell or organism, by at least 50% at least 72 hours post-administration of said dsRNA to a cell or organism, by at least 50% at least four, five or seven days post-administration of said dsRNA to a cell or organism, by at least 80% at least 48 hours post-administration of said dsRNA to a cell or organism, by at least 80% at least 72 hours post-administration of said dsRNA to a cell or organism, or by at least 80% at least four, five or seven days post-administration of said dsRNA to a cell or organism.

The dsRNA molecule can be designed such that every residue of the antisense strand is complementary to a residue in the target molecule. Alternatively, substitutions can be made within the molecule to increase stability and/or enhance processing activity of said molecule. Substitutions can be made within the strand or can be made to residues at the ends of the strand. In certain embodiments, substitutions and/or modifications are made at specific residues within a DsiRNA agent. Such substitutions and/or modifications can include, *e.g.*, deoxy- modifications at one or more residues of positions 1, 2 and 3 when numbering from the 3' terminal position of the sense strand of a DsiRNA agent; and introduction of 2'-O-alkyl (*e.g.*, 2'-O-methyl) modifications at the 3' terminal residue of the antisense strand of DsiRNA agents, with such modifications also being performed at overhang positions of the 3' portion of the antisense strand and at alternating residues of the antisense strand of the DsiRNA that are included within the region of a DsiRNA agent that is processed to form an active siRNA agent. The preceding modifications are offered as exemplary, and are not intended to be limiting in any manner. Further consideration of the structure of preferred DsiRNA agents, including further description of the modifications and substitutions that can be performed upon the anti-EGFR DsiRNA agents of the instant invention, can be found below.

Where a first sequence is referred to as "substantially complementary" with respect to

a second sequence herein, the two sequences can be fully complementary, or they may form one or more, but generally not more than 4, 3 or 2 mismatched base pairs upon hybridization, while retaining the ability to hybridize under the conditions most relevant to their ultimate application. However, where two oligonucleotides are designed to form, upon hybridization, one or more single stranded overhangs, such overhangs shall not be regarded as mismatches with regard to the determination of complementarity. For example, a dsRNA comprising one oligonucleotide 21 nucleotides in length and another oligonucleotide 23 nucleotides in length, wherein the longer oligonucleotide comprises a sequence of 21 nucleotides that is fully complementary to the shorter oligonucleotide, may yet be referred to as "fully complementary" for the purposes of the invention.

The term "double-stranded RNA" or "dsRNA", as used herein, refers to a complex of ribonucleic acid molecules, having a duplex structure comprising two anti-parallel and substantially complementary, as defined above, nucleic acid strands. The two strands forming the duplex structure may be different portions of one larger RNA molecule, or they may be separate RNA molecules. Where separate RNA molecules, such dsRNA are often referred to as siRNA ("short interfering RNA") or DsiRNA ("Dicer substrate siRNAs"). Where the two strands are part of one larger molecule, and therefore are connected by an uninterrupted chain of nucleotides between the 3'-end of one strand and the 5' end of the respective other strand forming the duplex structure, the connecting RNA chain is referred to as a "hairpin loop", "short hairpin RNA" or "shRNA". Where the two strands are connected covalently by means other than an uninterrupted chain of nucleotides between the 3'-end of one strand and the 5'end of the respective other strand forming the duplex structure, the connecting structure is referred to as a "linker". The RNA strands may have the same or a different number of nucleotides. The maximum number of base pairs is the number of nucleotides in the shortest strand of the dsRNA minus any overhangs that are present in the duplex. In addition to the duplex structure, a dsRNA may comprise one or more nucleotide overhangs. In addition, as used herein, "dsRNA" may include chemical modifications to ribonucleotides, internucleoside linkages, end-groups, caps, and conjugated moieties, including substantial modifications at multiple nucleotides and including all types of modifications disclosed herein or known in the art. Any such modifications, as used in an siRNA- or DsiRNA-type molecule, are encompassed by "dsRNA" for the purposes of this specification and claims.

The phrase "duplex region" refers to the region in two complementary or substantially complementary oligonucleotides that form base pairs with one another, either by Watson-Crick base pairing or other manner that allows for a duplex between oligonucleotide strands that are complementary or substantially complementary. For example, an oligonucleotide strand having 21 nucleotide units can base pair with another oligonucleotide of 21 nucleotide units, yet only 19 bases on each strand are complementary or substantially complementary, such that the "duplex region" consists of 19 base pairs. The remaining base pairs may, for example, exist as 5' and 3' overhangs. Further, within the duplex region, 100% complementarity is not required; substantial complementarity is allowable within a duplex region. Substantial complementarity refers to complementarity between the strands such that they are capable of annealing under biological conditions. Techniques to empirically determine if two strands are capable of annealing under biological conditions are well known in the art. Alternatively, two strands can be synthesized and added together under biological conditions to determine if they anneal to one another.

Single-stranded nucleic acids that base pair over a number of bases are said to "hybridize." Hybridization is typically determined under physiological or biologically relevant conditions (e.g., intracellular: pH 7.2, 140 mM potassium ion; extracellular pH 7.4, 145 mM sodium ion). Hybridization conditions generally contain a monovalent cation and biologically acceptable buffer and may or may not contain a divalent cation, complex anions, e.g. gluconate from potassium gluconate, uncharged species such as sucrose, and inert polymers to reduce the activity of water in the sample, e.g. PEG. Such conditions include conditions under which base pairs can form.

Hybridization is measured by the temperature required to dissociate single stranded nucleic acids forming a duplex, *i.e.*, (the melting temperature; T_m). Hybridization conditions are also conditions under which base pairs can form. Various conditions of stringency can be used to determine hybridization (see, e.g., Wahl, G. M. and S. L. Berger (1987) *Methods Enzymol.* 152:399; Kimmel, A. R. (1987) *Methods Enzymol.* 152:507). Stringent temperature conditions will ordinarily include temperatures of at least about 30° C, more preferably of at least about 37° C, and most preferably of at least about 42° C. The hybridization temperature for hybrids anticipated to be less than 50 base pairs in length should be 5-10°C less than the melting temperature (T_m) of the hybrid, where T_m is determined according to the following equations. For hybrids less than 18 base pairs in length, $T_m(^{\circ}\text{C})=2(\text{\# of A+T bases})+4(\text{\# of G+C bases})$. For hybrids between 18 and 49 base

pairs in length, $T_m(^{\circ}\text{C}) = 81.5 + 16.6(\log_{10}[\text{Na}^+]) + 0.41 (\% \text{ G+C}) - (600/\text{N})$, where N is the number of bases in the hybrid, and $[\text{Na}^+]$ is the concentration of sodium ions in the hybridization buffer ($[\text{Na}^+]$ for $1\times\text{SSC} = 0.165 \text{ M}$). For example, a hybridization determination buffer is shown in Table 1.

Table 1.

	final conc.	Vender	Cat#	Lot#	m.w./Stock	To make 50 mL solution
NaCl	100 mM	Sigma	S-5150	41K8934	5M	1 mL
KCl	80 mM	Sigma	P-9541	70K0002	74.55	0.298 g
MgCl ₂	8 mM	Sigma	M-1028	120K8933	1M	0.4 mL
sucrose	2% w/v	Fisher	BP220-212	907105	342.3	1 g
Tris-HCl	16 mM	Fisher	BP1757-500	12419	1M	0.8 mL
NaH ₂ PO ₄	1 mM	Sigma	S-3193	52H-029515	120.0	0.006 g
EDTA	0.02 mM	Sigma	E-7889	110K89271	0.5M	2 μL
H ₂ O		Sigma	W-4502	51K2359		to 50 mL
pH = 7.0 at 20°C	adjust with HCl					

Useful variations on hybridization conditions will be readily apparent to those skilled in the art. Hybridization techniques are well known to those skilled in the art and are described, for example, in Benton and Davis (Science 196:180, 1977); Grunstein and Hogness (Proc. Natl. Acad. Sci., USA 72:3961, 1975); Ausubel et al. (Current Protocols in Molecular Biology, Wiley Interscience, New York, 2001); Berger and Kimmel (Antisense to Molecular Cloning Techniques, 1987, Academic Press, New York); and Sambrook et al., Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratory Press, New York.

As used herein, "oligonucleotide strand" is a single stranded nucleic acid molecule. An oligonucleotide may comprise ribonucleotides, deoxyribonucleotides, modified nucleotides (*e.g.*, nucleotides with 2' modifications, synthetic base analogs, etc.) or combinations thereof. Such modified oligonucleotides can be preferred over native forms because of properties such as, for example, enhanced cellular uptake and increased stability in the presence of nucleases.

As used herein, the term "ribonucleotide" encompasses natural and synthetic, unmodified and modified ribonucleotides. Modifications include changes to the sugar moiety, to the base moiety and/or to the linkages between ribonucleotides in the oligonucleotide. As used herein, the term "ribonucleotide" specifically excludes a deoxyribonucleotide, which is a nucleotide possessing a single proton group at the 2' ribose

ring position.

As used herein, the term "deoxyribonucleotide" encompasses natural and synthetic, unmodified and modified deoxyribonucleotides. Modifications include changes to the sugar moiety, to the base moiety and/or to the linkages between deoxyribonucleotide in the oligonucleotide. As used herein, the term "deoxyribonucleotide" also includes a modified ribonucleotide that does not permit Dicer cleavage of a dsRNA agent, *e.g.*, a 2'-O-methyl ribonucleotide, a phosphorothioate-modified ribonucleotide residue, *etc.*, that does not permit Dicer cleavage to occur at a bond of such a residue.

As used herein, the term "PS-NA" refers to a phosphorothioate-modified nucleotide residue. The term "PS-NA" therefore encompasses both phosphorothioate-modified ribonucleotides ("PS-RNAs") and phosphorothioate-modified deoxyribonucleotides ("PS-DNAs").

As used herein, "Dicer" refers to an endoribonuclease in the RNase III family that cleaves a dsRNA or dsRNA-containing molecule, *e.g.*, double-stranded RNA (dsRNA) or pre-microRNA (miRNA), into double-stranded nucleic acid fragments 19-25 nucleotides long, usually with a two-base overhang on the 3' end. With respect to certain dsRNAs of the invention (*e.g.*, "DsiRNAs"), the duplex formed by a dsRNA region of an agent of the invention is recognized by Dicer and is a Dicer substrate on at least one strand of the duplex. Dicer catalyzes the first step in the RNA interference pathway, which consequently results in the degradation of a target RNA. The protein sequence of human Dicer is provided at the NCBI database under accession number NP_085124, hereby incorporated by reference.

Dicer "cleavage" can be determined as follows (*e.g.*, see Collingwood *et al.*, Oligonucleotides 18:187–200 (2008)). In a Dicer cleavage assay, RNA duplexes (100 pmol) are incubated in 20 μ L of 20 mM Tris pH 8.0, 200 mM NaCl, 2.5 mM MgCl₂ with or without 1 unit of recombinant human Dicer (Stratagene, La Jolla, CA) at 37°C for 18–24 hours. Samples are desalted using a Performa SR 96-well plate (Edge Biosystems, Gaithersburg, MD). Electrospray-ionization liquid chromatography mass spectroscopy (ESI-LCMS) of duplex RNAs pre- and post-treatment with Dicer is done using an Oligo HTCS system (Novatia, Princeton, NJ; Hail *et al.*, 2004), which consists of a ThermoFinnigan TSQ7000, Xcalibur data system, ProMass data processing software and Paradigm MS4 HPLC (Michrom BioResources, Auburn, CA). In this assay, Dicer cleavage occurs where at least 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95%, or even 100% of the Dicer

substrate dsRNA, (i.e., 25-30 bp, dsRNA, preferably 26-30 bp dsRNA) is cleaved to a shorter dsRNA (e.g., 19-23 bp dsRNA, preferably, 21-23 bp dsRNA).

As used herein, "Dicer cleavage site" refers to the sites at which Dicer cleaves a dsRNA (e.g., the dsRNA region of a DsiRNA agent of the invention). Dicer contains two RNase III domains which typically cleave both the sense and antisense strands of a dsRNA. The average distance between the RNase III domains and the PAZ domain determines the length of the short double-stranded nucleic acid fragments it produces and this distance can vary (Macrae *et al.* (2006) *Science* 311: 195–8). As shown in Figure 1, Dicer is projected to cleave certain double-stranded ribonucleic acids of the instant invention that possess an antisense strand having a 2 nucleotide 3' overhang at a site between the 21st and 22nd nucleotides removed from the 3' terminus of the antisense strand, and at a corresponding site between the 21st and 22nd nucleotides removed from the 5' terminus of the sense strand. The projected and/or prevalent Dicer cleavage site(s) for dsRNA molecules distinct from those depicted in Figure 1 may be similarly identified *via* art-recognized methods, including those described in Macrae *et al.* While the Dicer cleavage events depicted in Figure 1 generate 21 nucleotide siRNAs, it is noted that Dicer cleavage of a dsRNA (e.g., DsiRNA) can result in generation of Dicer-processed siRNA lengths of 19 to 23 nucleotides in length. Indeed, in certain embodiments, a double-stranded DNA region may be included within a dsRNA for purpose of directing prevalent Dicer excision of a typically non-preferred 19mer or 20mer siRNA, rather than a 21mer.

As used herein, "overhang" refers to unpaired nucleotides, in the context of a duplex having one or more free ends at the 5' terminus or 3' terminus of a dsRNA. In certain embodiments, the overhang is a 3' or 5' overhang on the antisense strand or sense strand. In some embodiments, the overhang is a 3' overhang having a length of between one and six nucleotides, optionally one to five, one to four, one to three, one to two, two to six, two to five, two to four, two to three, three to six, three to five, three to four, four to six, four to five, five to six nucleotides, or one, two, three, four, five or six nucleotides. "Blunt" or "blunt end" means that there are no unpaired nucleotides at that end of the dsRNA, i.e., no nucleotide overhang. For clarity, chemical caps or non-nucleotide chemical moieties conjugated to the 3' end or 5' end of an siRNA are not considered in determining whether an siRNA has an overhang or is blunt ended. In certain embodiments, the invention provides a dsRNA molecule for inhibiting the expression of the EGFR target gene in a cell or mammal, wherein the dsRNA comprises an antisense strand comprising a region of complementarity which is

complementary to at least a part of an mRNA formed in the expression of the EGFR target gene, and wherein the region of complementarity is less than 35 nucleotides in length, optionally 19-24 nucleotides in length or 25-30 nucleotides in length, and wherein the dsRNA, upon contact with a cell expressing the EGFR target gene, inhibits the expression of the EGFR target gene by at least 10%, 25%, or 40%.

A dsRNA of the invention comprises two RNA strands that are sufficiently complementary to hybridize to form a duplex structure. One strand of the dsRNA (the antisense strand) comprises a region of complementarity that is substantially complementary, and generally fully complementary, to a target sequence, derived from the sequence of an mRNA formed during the expression of the EGFR target gene, the other strand (the sense strand) comprises a region which is complementary to the antisense strand, such that the two strands hybridize and form a duplex structure when combined under suitable conditions. Generally, the duplex structure is between 15 and 35, optionally between 25 and 30, between 26 and 30, between 18 and 25, between 19 and 24, or between 19 and 21 base pairs in length. Similarly, the region of complementarity to the target sequence is between 15 and 35, optionally between 18 and 30, between 25 and 30, between 19 and 24, or between 19 and 21 nucleotides in length. The dsRNA of the invention may further comprise one or more single-stranded nucleotide overhang(s). It has been identified that dsRNAs comprising duplex structures of between 15 and 35 base pairs in length can be effective in inducing RNA interference, including DsiRNAs (generally of at least 25 base pairs in length) and siRNAs (in certain embodiments, duplex structures of siRNAs are between 20 and 23, and optionally, specifically 21 base pairs (Elbashir *et al.*, *EMBO* 20: 6877-6888)). It has also been identified that dsRNAs possessing duplexes shorter than 20 base pairs can be effective as well (*e.g.*, 15, 16, 17, 18 or 19 base pair duplexes). In certain embodiments, the dsRNAs of the invention can comprise at least one strand of a length of 19 nucleotides or more. In certain embodiments, it can be reasonably expected that shorter dsRNAs comprising a sequence complementary to one of the sequences of Table 6, minus only a few nucleotides on one or both ends may be similarly effective as compared to the dsRNAs described above and in Tables 2-5 and 7-10. Hence, dsRNAs comprising a partial sequence of at least 15, 16, 17, 18, 19, 20, or more contiguous nucleotides sufficiently complementary to one of the sequences of Table 6, and differing in their ability to inhibit the expression of the EGFR target gene in an assay as described herein by not more than 5, 10, 15, 20, 25, or 30% inhibition from a dsRNA comprising the full sequence, are contemplated by the invention. In one embodiment, at

least one end of the dsRNA has a single-stranded nucleotide overhang of 1 to 5, optionally 1 to 4, in certain embodiments, 1 or 2 nucleotides. Certain dsRNA structures having at least one nucleotide overhang possess superior inhibitory properties as compared to counterparts possessing base-paired blunt ends at both ends of the dsRNA molecule.

As used herein, the term "RNA processing" refers to processing activities performed by components of the siRNA, miRNA or RNase H pathways (*e.g.*, Drosha, Dicer, Argonaute2 or other RISC endoribonucleases, and RNaseH), which are described in greater detail below (see "RNA Processing" section below). The term is explicitly distinguished from the post-transcriptional processes of 5' capping of RNA and degradation of RNA *via* non-RISC- or non-RNase H-mediated processes. Such "degradation" of an RNA can take several forms, *e.g.* deadenylation (removal of a 3' poly(A) tail), and/or nuclease digestion of part or all of the body of the RNA by one or more of several endo- or exo-nucleases (*e.g.*, RNase III, RNase P, RNase T1, RNase A (1, 2, 3, 4/5), oligonucleotidase, etc.).

By "homologous sequence" is meant, a nucleotide sequence that is shared by one or more polynucleotide sequences, such as genes, gene transcripts and/or non-coding polynucleotides. For example, a homologous sequence can be a nucleotide sequence that is shared by two or more genes encoding related but different proteins, such as different members of a gene family, different protein epitopes, different protein isoforms or completely divergent genes, such as a cytokine and its corresponding receptors. A homologous sequence can be a nucleotide sequence that is shared by two or more non-coding polynucleotides, such as noncoding DNA or RNA, regulatory sequences, introns, and sites of transcriptional control or regulation. Homologous sequences can also include conserved sequence regions shared by more than one polynucleotide sequence. Homology does not need to be perfect homology (*e.g.*, 100%), as partially homologous sequences are also contemplated by the instant invention (*e.g.*, 99%, 98%, 97%, 96%, 95%, 94%, 93%, 92%, 91%, 90%, 89%, 88%, 87%, 86%, 85%, 84%, 83%, 82%, 81%, 80% etc.). Indeed, design and use of the dsRNA agents of the instant invention contemplates the possibility of using such dsRNA agents not only against target RNAs of EGFR possessing perfect complementarity with the presently described dsRNA agents, but also against target EGFR RNAs possessing sequences that are, *e.g.*, only 99%, 98%, 97%, 96%, 95%, 94%, 93%, 92%, 91%, 90%, 89%, 88%, 87%, 86%, 85%, 84%, 83%, 82%, 81%, 80% etc. complementary to said dsRNA agents. Similarly, it is contemplated that the presently described dsRNA agents of the instant invention might be readily altered by the skilled artisan to enhance the extent of complementarity between said

dsRNA agents and a target EGFR RNA, *e.g.*, of a specific allelic variant of EGFR (*e.g.*, an allele of enhanced therapeutic interest). Indeed, dsRNA agent sequences with insertions, deletions, and single point mutations relative to the target EGFR sequence can also be effective for inhibition. Alternatively, dsRNA agent sequences with nucleotide analog substitutions or insertions can be effective for inhibition.

Sequence identity may be determined by sequence comparison and alignment algorithms known in the art. To determine the percent identity of two nucleic acid sequences (or of two amino acid sequences), the sequences are aligned for comparison purposes (*e.g.*, gaps can be introduced in the first sequence or second sequence for optimal alignment). The nucleotides (or amino acid residues) at corresponding nucleotide (or amino acid) positions are then compared. When a position in the first sequence is occupied by the same residue as the corresponding position in the second sequence, then the molecules are identical at that position. The percent identity between the two sequences is a function of the number of identical positions shared by the sequences (i.e., % homology = # of identical positions / total # of positions x 100), optionally penalizing the score for the number of gaps introduced and/or length of gaps introduced.

The comparison of sequences and determination of percent identity between two sequences can be accomplished using a mathematical algorithm. In one embodiment, the alignment generated over a certain portion of the sequence aligned having sufficient identity but not over portions having low degree of identity (i.e., a local alignment). A preferred, non-limiting example of a local alignment algorithm utilized for the comparison of sequences is the algorithm of Karlin and Altschul (1990) *Proc. Natl. Acad. Sci. USA* 87:2264-68, modified as in Karlin and Altschul (1993) *Proc. Natl. Acad. Sci. USA* 90:5873-77. Such an algorithm is incorporated into the BLAST programs (version 2.0) of Altschul, et al. (1990) *J. Mol. Biol.* 215:403-10.

In another embodiment, a gapped alignment the alignment is optimized is formed by introducing appropriate gaps, and percent identity is determined over the length of the aligned sequences (i.e., a gapped alignment). To obtain gapped alignments for comparison purposes, Gapped BLAST can be utilized as described in Altschul et al., (1997) *Nucleic Acids Res.* 25(17):3389-3402. In another embodiment, a global alignment the alignment is optimized is formed by introducing appropriate gaps, and percent identity is determined over the entire length of the sequences aligned. (i.e., a global alignment). A preferred, non-limiting example of a mathematical algorithm utilized for the global comparison of sequences is the algorithm

of Myers and Miller, CABIOS (1989). Such an algorithm is incorporated into the ALIGN program (version 2.0) which is part of the GCG sequence alignment software package. When utilizing the ALIGN program for comparing amino acid sequences, a PAM120 weight residue table, a gap length penalty of 12, and a gap penalty of 4 can be used.

Greater than 80% sequence identity, e.g., 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or even 100% sequence identity, between the dsRNA antisense strand and the portion of the EGFR RNA sequence is preferred. Alternatively, the dsRNA may be defined functionally as a nucleotide sequence (or oligonucleotide sequence) that is capable of hybridizing with a portion of the EGFR RNA (e.g., 400 mM NaCl, 40 mM PIPES pH 6.4, 1 mM EDTA, 50°C or 70°C hybridization for 12-16 hours; followed by washing). Additional preferred hybridization conditions include hybridization at 70°C in 1xSSC or 50°C in 1xSSC, 50% formamide followed by washing at 70°C in 0.3xSSC or hybridization at 70°C in 4xSSC or 50°C in 4xSSC, 50% formamide followed by washing at 67°C in 1xSSC. The hybridization temperature for hybrids anticipated to be less than 50 base pairs in length should be 5-10°C less than the melting temperature (T_m) of the hybrid, where T_m is determined according to the following equations. For hybrids less than 18 base pairs in length, $T_m(^{\circ}\text{C})=2(\# \text{ of A+T bases})+4(\# \text{ of G+C bases})$. For hybrids between 18 and 49 base pairs in length, $T_m(^{\circ}\text{C})=81.5+16.6(\log_{10}[\text{Na}^+])+0.41(\% \text{ G+C})-(600/\text{N})$, where N is the number of bases in the hybrid, and $[\text{Na}^+]$ is the concentration of sodium ions in the hybridization buffer ($[\text{Na}^+]$ for 1xSSC=0.165 M). Additional examples of stringency conditions for polynucleotide hybridization are provided in Sambrook, J., E. F. Fritsch, and T. Maniatis, 1989, *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y., chapters 9 and 11, and *Current Protocols in Molecular Biology*, 1995, F. M. Ausubel et al., eds., John Wiley & Sons, Inc., sections 2.10 and 6.3-6.4. The length of the identical nucleotide sequences may be at least 10, 12, 15, 17, 20, 22, 25, 27 or 30 bases.

By "conserved sequence region" is meant, a nucleotide sequence of one or more regions in a polynucleotide does not vary significantly between generations or from one biological system, subject, or organism to another biological system, subject, or organism. The polynucleotide can include both coding and non-coding DNA and RNA.

By "sense region" is meant a nucleotide sequence of a dsRNA molecule having complementarity to an antisense region of the dsRNA molecule. In addition, the sense region

of a dsRNA molecule can comprise a nucleic acid sequence having homology with a target nucleic acid sequence.

By "antisense region" is meant a nucleotide sequence of a dsRNA molecule having complementarity to a target nucleic acid sequence. In addition, the antisense region of a dsRNA molecule comprises a nucleic acid sequence having complementarity to a sense region of the dsRNA molecule.

As used herein, "antisense strand" refers to a single stranded nucleic acid molecule which has a sequence complementary to that of a target RNA. When the antisense strand contains modified nucleotides with base analogs, it is not necessarily complementary over its entire length, but must at least hybridize with a target RNA.

As used herein, "sense strand" refers to a single stranded nucleic acid molecule which has a sequence complementary to that of an antisense strand. When the antisense strand contains modified nucleotides with base analogs, the sense strand need not be complementary over the entire length of the antisense strand, but must at least duplex with the antisense strand.

As used herein, "guide strand" refers to a single stranded nucleic acid molecule of a dsRNA or dsRNA-containing molecule, which has a sequence sufficiently complementary to that of a target RNA to result in RNA interference. After cleavage of the dsRNA or dsRNA-containing molecule by Dicer, a fragment of the guide strand remains associated with RISC, binds a target RNA as a component of the RISC complex, and promotes cleavage of a target RNA by RISC. As used herein, the guide strand does not necessarily refer to a continuous single stranded nucleic acid and may comprise a discontinuity, preferably at a site that is cleaved by Dicer. A guide strand is an antisense strand.

As used herein, "passenger strand" refers to an oligonucleotide strand of a dsRNA or dsRNA-containing molecule, which has a sequence that is complementary to that of the guide strand. As used herein, the passenger strand does not necessarily refer to a continuous single stranded nucleic acid and may comprise a discontinuity, preferably at a site that is cleaved by Dicer. A passenger strand is a sense strand.

By "target nucleic acid" is meant a nucleic acid sequence whose expression, level or activity is to be modulated. The target nucleic acid can be DNA or RNA. For agents that target EGFR, in certain embodiments, the target nucleic acid is EGFR RNA. EGFR RNA target sites can also interchangeably be referenced by corresponding cDNA sequences. Levels of EGFR may also be targeted *via* targeting of upstream effectors of EGFR, or the

effects of modulated or misregulated EGFR may also be modulated by targeting of molecules downstream of EGFR in the EGFR signalling pathway.

By "complementarity" is meant that a nucleic acid can form hydrogen bond(s) with another nucleic acid sequence by either traditional Watson-Crick or other non-traditional types. In reference to the nucleic molecules of the present invention, the binding free energy for a nucleic acid molecule with its complementary sequence is sufficient to allow the relevant function of the nucleic acid to proceed, e.g., RNAi activity. Determination of binding free energies for nucleic acid molecules is well known in the art (see, e.g., Turner et al., 1987, CSH Symp. Quant. Biol. LII pp. 123-133; Frier et al., 1986, Proc. Nat. Acad. Sci. USA 83:9373-9377; Turner et al., 1987, J. Am. Chem. Soc. 109:3783-3785). A percent complementarity indicates the percentage of contiguous residues in a nucleic acid molecule that can form hydrogen bonds (e.g., Watson-Crick base pairing) with a second nucleic acid sequence (e.g., 5, 6, 7, 8, 9, or 10 nucleotides out of a total of 10 nucleotides in the first oligonucleotide being based paired to a second nucleic acid sequence having 10 nucleotides represents 50%, 60%, 70%, 80%, 90%, and 100% complementary respectively). "Perfectly complementary" means that all the contiguous residues of a nucleic acid sequence will hydrogen bond with the same number of contiguous residues in a second nucleic acid sequence. In one embodiment, a dsRNA molecule of the invention comprises 19 to 30 (e.g., 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, or 30 or more) nucleotides that are complementary to one or more target nucleic acid molecules or a portion thereof.

In one embodiment, dsRNA molecules of the invention that down regulate or reduce EGFR gene expression are used for treating, preventing or reducing EGFR-related diseases or disorders (e.g., cancer) in a subject or organism.

In one embodiment of the present invention, each sequence of a DsiRNA molecule of the invention is independently 25 to 35 nucleotides in length, in specific embodiments 25, 26, 27, 28, 29, 30, 31, 32, 33, 34 or 35 nucleotides in length. In another embodiment, the DsiRNA duplexes of the invention independently comprise 25 to 30 base pairs (e.g., 25, 26, 27, 28, 29, or 30). In another embodiment, one or more strands of the DsiRNA molecule of the invention independently comprises 19 to 35 nucleotides (e.g., 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34 or 35) that are complementary to a target (EGFR) nucleic acid molecule. In certain embodiments, a DsiRNA molecule of the invention possesses a length of duplexed nucleotides between 25 and 34 nucleotides in length (e.g., 25, 26, 27, 28, 29, 30, 31, 32, 33 or 34 nucleotides in length; optionally, all such nucleotides base pair with

cognate nucleotides of the opposite strand). (Exemplary DsiRNA molecules of the invention are shown in Figure 1, and below.

As used herein "cell" is used in its usual biological sense, and does not refer to an entire multicellular organism, e.g., specifically does not refer to a human. The cell can be present in an organism, e.g., birds, plants and mammals such as humans, cows, sheep, apes, monkeys, swine, dogs, and cats. The cell can be prokaryotic (e.g., bacterial cell) or eukaryotic (e.g., mammalian or plant cell). The cell can be of somatic or germ line origin, totipotent or pluripotent, dividing or non-dividing. The cell can also be derived from or can comprise a gamete or embryo, a stem cell, or a fully differentiated cell. Within certain aspects, the term "cell" refers specifically to mammalian cells, such as human cells, that contain one or more isolated dsRNA molecules of the present disclosure. In particular aspects, a cell processes dsRNAs or dsRNA-containing molecules resulting in RNA interference of target nucleic acids, and contains proteins and protein complexes required for RNAi, e.g., Dicer and RISC.

In certain embodiments, dsRNAs of the invention are Dicer substrate siRNAs ("DsiRNAs"). DsiRNAs can possess certain advantages as compared to inhibitory nucleic acids that are not dicer substrates ("non-DsiRNAs"). Such advantages include, but are not limited to, enhanced duration of effect of a DsiRNA relative to a non-DsiRNA, as well as enhanced inhibitory activity of a DsiRNA as compared to a non-DsiRNA (e.g., a 19-23mer siRNA) when each inhibitory nucleic acid is suitably formulated and assessed for inhibitory activity in a mammalian cell at the same concentration (in this latter scenario, the DsiRNA would be identified as more potent than the non-DsiRNA). Detection of the enhanced potency of a DsiRNA relative to a non-DsiRNA is often most readily achieved at a formulated concentration (e.g., transfection concentration of the dsRNA) that results in the DsiRNA eliciting approximately 30-70% knockdown activity upon a target RNA (e.g., a mRNA). For active DsiRNAs, such levels of knockdown activity are most often achieved at *in vitro* mammalian cell DsiRNA transfection concentrations of 1 nM or less of as suitably formulated, and in certain instances are observed at DsiRNA transfection concentrations of 200 pM or less, 100 pM or less, 50pM or less, 20 pM or less, 10 pM or less, 5 pM or less, or even 1 pM or less. Indeed, due to the variability among DsiRNAs of the precise concentration at which 30-70% knockdown of a target RNA is observed, construction of an IC₅₀ curve *via* assessment of the inhibitory activity of DsiRNAs and non-DsiRNAs across a range of effective concentrations is a preferred method for detecting the enhanced potency of

a DsiRNA relative to a non-DsiRNA inhibitory agent.

In certain embodiments, a DsiRNA (in a state as initially formed, prior to dicer cleavage) is more potent at reducing EGFR target gene expression in a mammalian cell than a 19, 20, 21, 22 or 23 base pair sequence that is contained within it. In certain such embodiments, a DsiRNA prior to dicer cleavage is more potent than a 19-21mer contained within it. Optionally, a DsiRNA prior to dicer cleavage is more potent than a 19 base pair duplex contained within it that is synthesized with symmetric dTdT overhangs (thereby forming a siRNA possessing 21 nucleotide strand lengths having dTdT overhangs). In certain embodiments, the DsiRNA is more potent than a 19-23mer siRNA (e.g., a 19 base pair duplex with dTdT overhangs) that targets at least 15 nucleotides of the 21 nucleotide target sequence that is recited for a DsiRNA of the invention (without wishing to be bound by theory, the identity of a such a target site for a DsiRNA is identified *via* identification of the Ago2 cleavage site for the DsiRNA; once the Ago2 cleavage site of a DsiRNA is determined for a DsiRNA, identification of the Ago2 cleavage site for any other inhibitory dsRNA can be performed and these Ago2 cleavage sites can be aligned, thereby determining the alignment of projected target nucleotide sequences for multiple dsRNAs). In certain related embodiments, the DsiRNA is more potent than a 19-23mer siRNA that targets at least 20 nucleotides of the 21 nucleotide target sequence that is recited for a DsiRNA of the invention. Optionally, the DsiRNA is more potent than a 19-23mer siRNA that targets the same 21 nucleotide target sequence that is recited for a DsiRNA of the invention. In certain embodiments, the DsiRNA is more potent than any 21mer siRNA that targets the same 21 nucleotide target sequence that is recited for a DsiRNA of the invention. Optionally, the DsiRNA is more potent than any 21 or 22mer siRNA that targets the same 21 nucleotide target sequence that is recited for a DsiRNA of the invention. In certain embodiments, the DsiRNA is more potent than any 21, 22 or 23mer siRNA that targets the same 21 nucleotide target sequence that is recited for a DsiRNA of the invention. As noted above, such potency assessments are most effectively performed upon dsRNAs that are suitably formulated (e.g., formulated with an appropriate transfection reagent) at a concentration of 1 nM or less. Optionally, an IC₅₀ assessment is performed to evaluate activity across a range of effective inhibitory concentrations, thereby allowing for robust comparison of the relative potencies of dsRNAs so assayed.

The dsRNA molecules of the invention are added directly, or can be complexed with lipids (e.g., cationic lipids), packaged within liposomes, or otherwise delivered to target cells

or tissues. The nucleic acid or nucleic acid complexes can be locally administered to relevant tissues *ex vivo*, or *in vivo* through direct dermal application, transdermal application, or injection, with or without their incorporation in biopolymers. In particular embodiments, the nucleic acid molecules of the invention comprise sequences shown in Figure 1, and the below exemplary structures. Examples of such nucleic acid molecules consist essentially of sequences defined in these figures and exemplary structures. Furthermore, where such agents are modified in accordance with the below description of modification patterning of DsiRNA agents, chemically modified forms of constructs described in Figure 1, and the below exemplary structures can be used in all uses described for the DsiRNA agents of Figure 1, and the below exemplary structures.

In another aspect, the invention provides mammalian cells containing one or more dsRNA molecules of this invention. The one or more dsRNA molecules can independently be targeted to the same or different sites.

By "RNA" is meant a molecule comprising at least one, and preferably at least 4, 8 and 12 ribonucleotide residues. The at least 4, 8 or 12 RNA residues may be contiguous. By "ribonucleotide" is meant a nucleotide with a hydroxyl group at the 2' position of a β -D-ribofuranose moiety. The terms include double-stranded RNA, single-stranded RNA, isolated RNA such as partially purified RNA, essentially pure RNA, synthetic RNA, recombinantly produced RNA, as well as altered RNA that differs from naturally occurring RNA by the addition, deletion, substitution and/or alteration of one or more nucleotides. Such alterations can include addition of non-nucleotide material, such as to the end(s) of the dsRNA or internally, for example at one or more nucleotides of the RNA. Nucleotides in the RNA molecules of the instant invention can also comprise non-standard nucleotides, such as non-naturally occurring nucleotides or chemically synthesized nucleotides or deoxynucleotides. These altered RNAs can be referred to as analogs or analogs of naturally-occurring RNA.

By "subject" is meant an organism, which is a donor or recipient of explanted cells or the cells themselves. "Subject" also refers to an organism to which the dsRNA agents of the invention can be administered. A subject can be a mammal or mammalian cells, including a human or human cells.

The phrase "pharmaceutically acceptable carrier" refers to a carrier for the administration of a therapeutic agent. Exemplary carriers include saline, buffered saline, dextrose, water, glycerol, ethanol, and combinations thereof. For drugs administered orally,

pharmaceutically acceptable carriers include, but are not limited to pharmaceutically acceptable excipients such as inert diluents, disintegrating agents, binding agents, lubricating agents, sweetening agents, flavoring agents, coloring agents and preservatives. Suitable inert diluents include sodium and calcium carbonate, sodium and calcium phosphate, and lactose, while corn starch and alginic acid are suitable disintegrating agents. Binding agents may include starch and gelatin, while the lubricating agent, if present, will generally be magnesium stearate, stearic acid or talc. If desired, the tablets may be coated with a material such as glyceryl monostearate or glyceryl distearate, to delay absorption in the gastrointestinal tract. The pharmaceutically acceptable carrier of the disclosed dsRNA compositions may be micellar structures, such as a liposomes, capsids, capsoids, polymeric nanocapsules, or polymeric microcapsules.

Polymeric nanocapsules or microcapsules facilitate transport and release of the encapsulated or bound dsRNA into the cell. They include polymeric and monomeric materials, especially including polybutylcyanoacrylate. A summary of materials and fabrication methods has been published (see Kreuter, 1991). The polymeric materials which are formed from monomeric and/or oligomeric precursors in the polymerization/nanoparticle generation step, are *per se* known from the prior art, as are the molecular weights and molecular weight distribution of the polymeric material which a person skilled in the field of manufacturing nanoparticles may suitably select in accordance with the usual skill.

Various methodologies of the instant invention include step that involves comparing a value, level, feature, characteristic, property, etc. to a "suitable control", referred to interchangeably herein as an "appropriate control". A "suitable control" or "appropriate control" is a control or standard familiar to one of ordinary skill in the art useful for comparison purposes. In one embodiment, a "suitable control" or "appropriate control" is a value, level, feature, characteristic, property, etc. determined prior to performing an RNAi methodology, as described herein. For example, a transcription rate, mRNA level, translation rate, protein level, biological activity, cellular characteristic or property, genotype, phenotype, etc. can be determined prior to introducing an RNA silencing agent (*e.g.*, DsiRNA) of the invention into a cell or organism. In another embodiment, a "suitable control" or "appropriate control" is a value, level, feature, characteristic, property, etc. determined in a cell or organism, *e.g.*, a control or normal cell or organism, exhibiting, for example, normal traits. In yet another embodiment, a "suitable control" or "appropriate control" is a predefined value, level, feature, characteristic, property, etc.

The term "*in vitro*" has its art recognized meaning, *e.g.*, involving purified reagents or extracts, *e.g.*, cell extracts. The term "*in vivo*" also has its art recognized meaning, *e.g.*, involving living cells, *e.g.*, immortalized cells, primary cells, cell lines, and/or cells in an organism.

"Treatment", or "treating" as used herein, is defined as the application or administration of a therapeutic agent (*e.g.*, a dsRNA agent or a vector or transgene encoding same) to a patient, or application or administration of a therapeutic agent to an isolated tissue or cell line from a patient, who has a disorder with the purpose to cure, heal, alleviate, relieve, alter, remedy, ameliorate, improve or affect the disease or disorder, or symptoms of the disease or disorder. The term "treatment" or "treating" is also used herein in the context of administering agents prophylactically. The term "effective dose" or "effective dosage" is defined as an amount sufficient to achieve or at least partially achieve the desired effect. The term "therapeutically effective dose" is defined as an amount sufficient to cure or at least partially arrest the disease and its complications in a patient already suffering from the disease. The term "patient" includes human and other mammalian subjects that receive either prophylactic or therapeutic treatment.

Structures of Anti-EGFR DsiRNA Agents

In certain embodiments, the anti-EGFR DsiRNA agents of the invention can have the following structures:

In one such embodiment, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-3'
3' -YXXXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA and "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers. In a related embodiment, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXDD-3'
3' -YXXXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers, and "D"=DNA. In one embodiment, the top strand is the sense strand, and the bottom strand is the antisense strand. Alternatively, the bottom strand is the sense strand and the top strand is the antisense strand.

DsiRNAs of the invention can carry a broad range of modification patterns (*e.g.*, 2'-O-

methyl RNA patterns, *e.g.*, within extended DsiRNA agents). Certain modification patterns of the second strand of DsiRNAs of the invention are presented below.

In one embodiment, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-3'

3' -YXXXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers and underlined residues are 2'-O-methyl RNA monomers. In a related embodiment, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXDD-3'

3' -YXXXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers and underlined residues are 2'-O-methyl RNA monomers, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand.

In another such embodiment, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-3'

3' -YXXXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers and underlined residues are 2'-O-methyl RNA monomers. In a related embodiment, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXDD-3'

3' -YXXXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers, underlined residues are 2'-O-methyl RNA monomers, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand.

In another such embodiment, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-3'

3' -YXXXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers and underlined residues are 2'-O-methyl RNA monomers. In a related embodiment, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXDD-3'
 3' -YXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers, underlined residues are 2'-O-methyl RNA monomers, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand.

In further embodiments, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXX-3'
 3' -YXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers and underlined residues are 2'-O-methyl RNA monomers. In a related embodiment, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXDD-3'
 3' -YXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers, underlined residues are 2'-O-methyl RNA monomers, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In one related embodiment, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXX-3'
 3' -XXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA and "X"=2'-O-methyl RNA. In a further related embodiment, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXDD-3'
 3' -XXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. This modification pattern is also referred to herein as the "AS-M7" or "M7" modification pattern.

In additional embodiments, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXX-3'
 3' -YXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers and underlined residues are

2'-O-methyl RNA monomers. In a related embodiment, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXDD-3'

3' -YXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers, underlined residues are 2'-O-methyl RNA monomers, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In another related embodiment, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXX-3'

3' -XXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA and "X"=2'-O-methyl RNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In a further related embodiment, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXDD-3'

3' -XXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. This modification pattern is also referred to herein as the "AS-M6" or "M6" modification pattern.

In other embodiments, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXX-3'

3' -YXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers and underlined residues are 2'-O-methyl RNA monomers. The top strand is the sense strand, and the bottom strand is the antisense strand. In a related embodiment, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXDD-3'

3' -YXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers, underlined residues are 2'-O-methyl RNA monomers, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In one related embodiment, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXX-3'

3' - XXXXXXXXXXXXXXXXXXXXXXXXXXXX - 5'

wherein "X"=RNA and "X"=2'-O-methyl RNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In another related embodiment, the DsiRNA comprises:

5' - XXXXXXXXXXXXXXXXXXXXXXXXXXXXDD - 3'

3' - XXXXXXXXXXXXXXXXXXXXXXXXXXXX - 5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. This modification pattern is also referred to herein as the "AS-M5" or "M5" modification pattern.

In further embodiments, the DsiRNA comprises:

5' - XXXXXXXXXXXXXXXXXXXXXXXXXXXX - 3'

3' - YXXXXXXXXXXXXXXXXXXXXXXXXX - 5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers and underlined residues are 2'-O-methyl RNA monomers. The top strand is the sense strand, and the bottom strand is the antisense strand. In a related embodiment, the DsiRNA comprises:

5' - XXXXXXXXXXXXXXXXXXXXXXXXXXXXDD - 3'

3' - YXXXXXXXXXXXXXXXXXXXXXXXXX - 5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers, underlined residues are 2'-O-methyl RNA monomers, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In one related embodiment, the DsiRNA comprises:

5' - XXXXXXXXXXXXXXXXXXXXXXXXXXXX - 3'

3' - XXXXXXXXXXXXXXXXXXXXXXXXXXXX - 5'

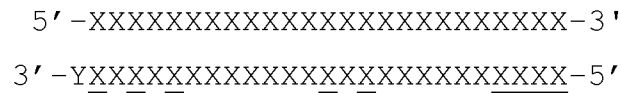
wherein "X"=RNA and "X"=2'-O-methyl RNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In a further related embodiment, the DsiRNA comprises:

5' - XXXXXXXXXXXXXXXXXXXXXXXXXXXXDD - 3'

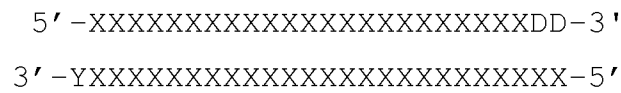
3' - XXXXXXXXXXXXXXXXXXXXXXXXXXXX - 5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. This modification pattern is also referred to herein as the "AS-M4" or "M4" modification pattern.

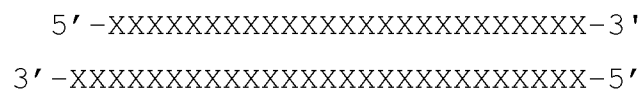
In additional embodiments, the DsiRNA comprises:



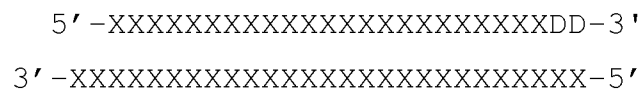
wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers and underlined residues are 2'-O-methyl RNA monomers. The top strand is the sense strand, and the bottom strand is the antisense strand. In a related embodiment, the DsiRNA comprises:



wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers, underlined residues are 2'-O-methyl RNA monomers, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In another related embodiment, the DsiRNA comprises:

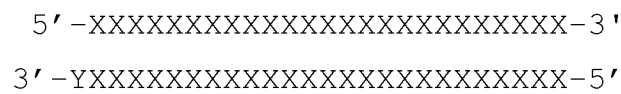


wherein "X"=RNA and "X"=2'-O-methyl RNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In a further related embodiment, the DsiRNA comprises:

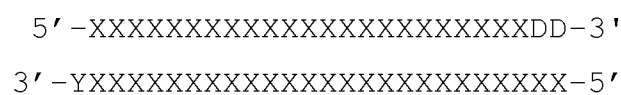


wherein "X"=RNA, "X"=2'-O-methyl RNA, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. This modification pattern is also referred to herein as the "AS-M8" or "M8" modification pattern.

In other embodiments, the DsiRNA comprises:



wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers and underlined residues are 2'-O-methyl RNA monomers. The top strand is the sense strand, and the bottom strand is the antisense strand. In one related embodiment, the DsiRNA comprises:



wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers, underlined residues are 2'-O-methyl RNA monomers, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In another related embodiment, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-3'
 3' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA and "X"=2'-O-methyl RNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In a further related embodiment, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXDD-3'
 3' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. This modification pattern is also referred to herein as the "AS-M3" or "M3" modification pattern.

In additional embodiments, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-3'
 3' -YXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers and underlined residues are 2'-O-methyl RNA monomers. The top strand is the sense strand, and the bottom strand is the antisense strand. In a related embodiment, the DsiRNA comprises:

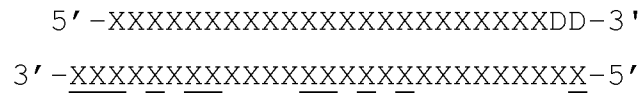
5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXDD-3'
 3' -YXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers, underlined residues are 2'-O-methyl RNA monomers, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In another related embodiment, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-3'
 3' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

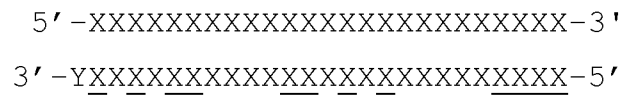
wherein "X"=RNA and "X"=2'-O-methyl RNA. The top strand is the sense strand, and the

bottom strand is the antisense strand. In a further related embodiment, the DsiRNA comprises:

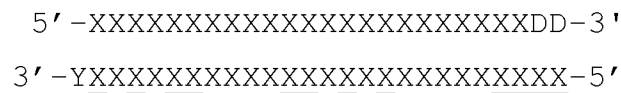


wherein "X"=RNA, "X"=2'-O-methyl RNA, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. This modification pattern is also referred to herein as the "AS-M2" or "M2" modification pattern.

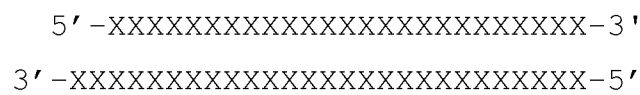
In further embodiments, the DsiRNA comprises:



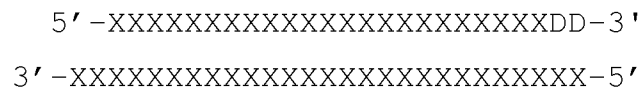
wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers and underlined residues are 2'-O-methyl RNA monomers. The top strand is the sense strand, and the bottom strand is the antisense strand. In a related embodiment, the DsiRNA comprises:



wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers, underlined residues are 2'-O-methyl RNA monomers, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In another related embodiment, the DsiRNA comprises:



wherein "X"=RNA and "X"=2'-O-methyl RNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In a further related embodiment, the DsiRNA comprises:



wherein "X"=RNA, "X"=2'-O-methyl RNA, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. This modification pattern is also referred to herein as the "AS-M1" or "M1" modification pattern.

In additional embodiments, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-3'
 3' -YXXXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers and underlined residues are 2'-O-methyl RNA monomers. The top strand is the sense strand, and the bottom strand is the antisense strand. In one related embodiment, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXDD-3'
 3' -YXXXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers, underlined residues are 2'-O-methyl RNA monomers, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In another related embodiment, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-3'
 3' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA and "X"=2'-O-methyl RNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In a further related embodiment, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXDD-3'
 3' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. This modification pattern is also referred to herein as the "AS-M9" or "M9" modification pattern.

In other embodiments, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-3'
 3' -YXXXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers and underlined residues are 2'-O-methyl RNA monomers. The top strand is the sense strand, and the bottom strand is the antisense strand. In a related embodiment, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXDD-3'
 3' -YXXXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an overhang domain comprised of 1-4

RNA monomers that are optionally 2'-O-methyl RNA monomers, underlined residues are 2'-O-methyl RNA monomers, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In another related embodiment, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-3'
 3' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA and "X"=2'-O-methyl RNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In a further related embodiment, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXDD-3'
 3' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. This modification pattern is also referred to herein as the "AS-M10" or "M10" modification pattern.

In further embodiments, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-3'
 3' -YXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers and underlined residues are 2'-O-methyl RNA monomers. The top strand is the sense strand, and the bottom strand is the antisense strand. In one related embodiment, the DsiRNA comprises:

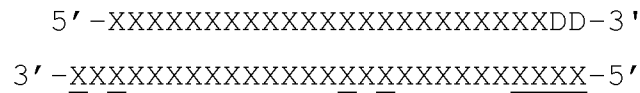
5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXDD-3'
 3' -YXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers, underlined residues are 2'-O-methyl RNA monomers, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In another related embodiment, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-3'
 3' -XXXXXXXXXXXXXXXXXXXX-5'

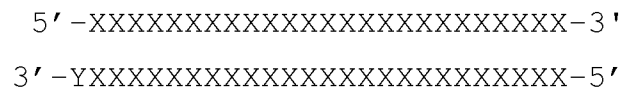
wherein "X"=RNA and "X"=2'-O-methyl RNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In a further related embodiment, the DsiRNA

comprises:

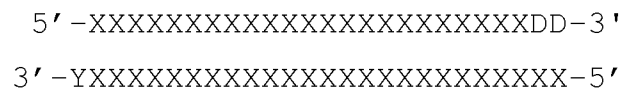


wherein "X"=RNA, "X"=2'-O-methyl RNA, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. This modification pattern is also referred to herein as the "AS-M11" or "M11" modification pattern.

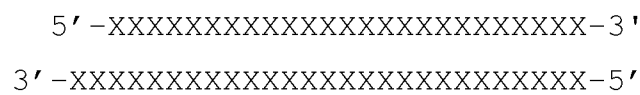
In additional embodiments, the DsiRNA comprises:



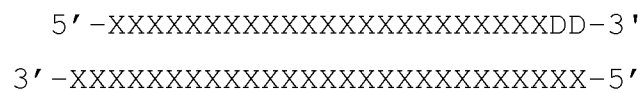
wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers and underlined residues are 2'-O-methyl RNA monomers. The top strand is the sense strand, and the bottom strand is the antisense strand. In one related embodiment, the DsiRNA comprises:



wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers, underlined residues are 2'-O-methyl RNA monomers, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In another related embodiment, the DsiRNA comprises:

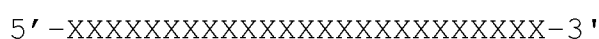


wherein "X"=RNA and "X"=2'-O-methyl RNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In a further related embodiment, the DsiRNA comprises:



wherein "X"=RNA, "X"=2'-O-methyl RNA, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. This modification pattern is also referred to herein as the "AS-M12" or "M12" modification pattern.

In further embodiments, the DsiRNA comprises:



3' - YXXXXXXXXXXXXXXXXXXXX - 5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers and underlined residues are 2'-O-methyl RNA monomers. The top strand is the sense strand, and the bottom strand is the antisense strand. In one related embodiment, the DsiRNA comprises:

5' - XXXXXXXXXXXXXXXXXXXXXXXDD - 3'

3' - YXXXXXXXXXXXXXXXXXXXX - 5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers, underlined residues are 2'-O-methyl RNA monomers, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In another related embodiment, the DsiRNA comprises:

5' - XXXXXXXXXXXXXXXXXXXXXXX - 3'

3' - XXXXXXXXXXXXXXXXXXXX - 5'

wherein "X"=RNA and "X"=2'-O-methyl RNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In a further related embodiment, the DsiRNA comprises:

5' - XXXXXXXXXXXXXXXXXXXXXXXDD - 3'

3' - XXXXXXXXXXXXXXXXXXXX - 5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. This modification pattern is also referred to herein as the "AS-M13" or "M13" modification pattern.

In other embodiments, the DsiRNA comprises:

5' - XXXXXXXXXXXXXXXXXXXXXXX - 3'

3' - YXXXXXXXXXXXXXXXXXXXX - 5'

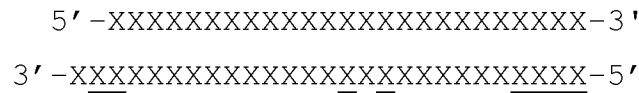
wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers and underlined residues are 2'-O-methyl RNA monomers. The top strand is the sense strand, and the bottom strand is the antisense strand. In another related embodiment, the DsiRNA comprises:

5' - XXXXXXXXXXXXXXXXXXXXXXXDD - 3'

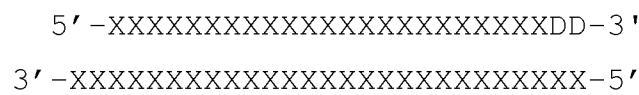
3' - YXXXXXXXXXXXXXXXXXXXX - 5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an overhang domain comprised of 1-4

RNA monomers that are optionally 2'-O-methyl RNA monomers, underlined residues are 2'-O-methyl RNA monomers, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In another related embodiment, the DsiRNA comprises:

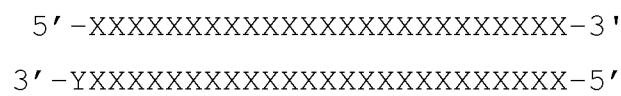


wherein "X"=RNA and "X"=2'-O-methyl RNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In a further related embodiment, the DsiRNA comprises:

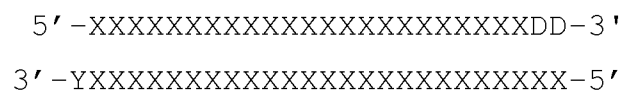


wherein "X"=RNA, "X"=2'-O-methyl RNA, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. This modification pattern is also referred to herein as the "AS-M21" or "M21" modification pattern.

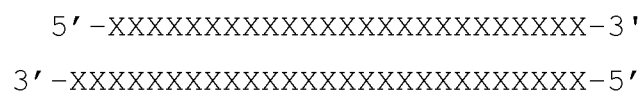
In further embodiments, the DsiRNA comprises:



wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers and underlined residues are 2'-O-methyl RNA monomers. The top strand is the sense strand, and the bottom strand is the antisense strand. In one related embodiment, the DsiRNA comprises:

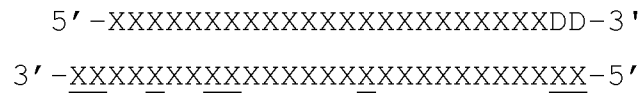


wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers, underlined residues are 2'-O-methyl RNA monomers, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In another related embodiment, the DsiRNA comprises:



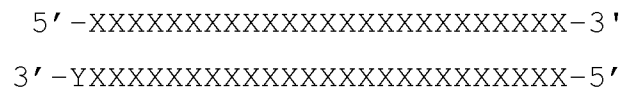
wherein "X"=RNA and "X"=2'-O-methyl RNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In a further related embodiment, the DsiRNA

comprises:

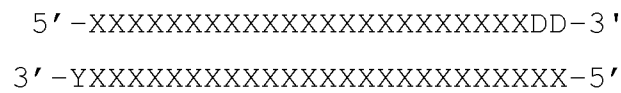


wherein "X"=RNA, "X"=2'-O-methyl RNA, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. This modification pattern is also referred to herein as the "AS-M14" or "M14" modification pattern.

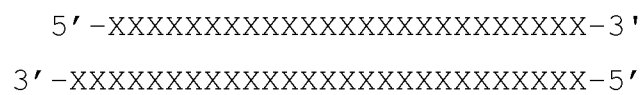
In additional embodiments, the DsiRNA comprises:



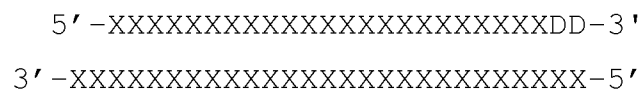
wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers and underlined residues are 2'-O-methyl RNA monomers. The top strand is the sense strand, and the bottom strand is the antisense strand. In one related embodiment, the DsiRNA comprises:



wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers, underlined residues are 2'-O-methyl RNA monomers, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In another related embodiment, the DsiRNA comprises:

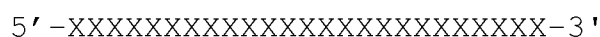


wherein "X"=RNA and "X"=2'-O-methyl RNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In a further related embodiment, the DsiRNA comprises:



wherein "X"=RNA, "X"=2'-O-methyl RNA, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. This modification pattern is also referred to herein as the "AS-M15" or "M15" modification pattern.

In further embodiments, the DsiRNA comprises:



3' - YXXXXXXXXXXXXXXXXXXXXX - 5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers and underlined residues are 2'-O-methyl RNA monomers. The top strand is the sense strand, and the bottom strand is the antisense strand. In a related embodiment, the DsiRNA comprises:

5' - XXXXXXXXXXXXXXXXXXXXXXXDD - 3'

3' - YXXXXXXXXXXXXXXXXXXXXX - 5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers, underlined residues are 2'-O-methyl RNA monomers, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In another related embodiment, the DsiRNA comprises:

5' - XXXXXXXXXXXXXXXXXXXXXXX - 3'

3' - XXXXXXXXXXXXXXXXXXXXX - 5'

wherein "X"=RNA and "X"=2'-O-methyl RNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In a further related embodiment, the DsiRNA comprises:

5' - XXXXXXXXXXXXXXXXXXXXXXXDD - 3'

3' - XXXXXXXXXXXXXXXXXXXXX - 5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. This modification pattern is also referred to herein as the "AS-M16" or "M16" modification pattern.

In additional embodiments, the DsiRNA comprises:

5' - XXXXXXXXXXXXXXXXXXXXXXX - 3'

3' - YXXXXXXXXXXXXXXXXXXXXX - 5'

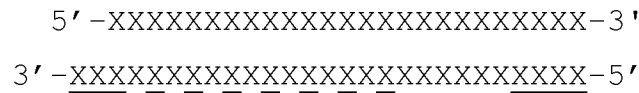
wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers and underlined residues are 2'-O-methyl RNA monomers. The top strand is the sense strand, and the bottom strand is the antisense strand. In one related embodiment, the DsiRNA comprises:

5' - XXXXXXXXXXXXXXXXXXXXXXXDD - 3'

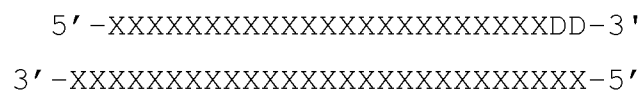
3' - YXXXXXXXXXXXXXXXXXXXXX - 5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an overhang domain comprised of 1-4

RNA monomers that are optionally 2'-O-methyl RNA monomers, underlined residues are 2'-O-methyl RNA monomers, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In another related embodiment, the DsiRNA comprises:

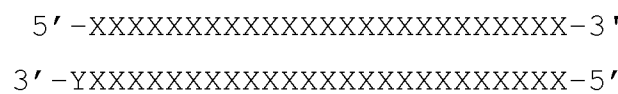


wherein "X"=RNA and "X"=2'-O-methyl RNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In a further related embodiment, the DsiRNA comprises:

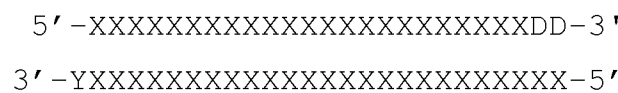


wherein "X"=RNA, "X"=2'-O-methyl RNA, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. This modification pattern is also referred to herein as the "AS-M17" or "M17" modification pattern.

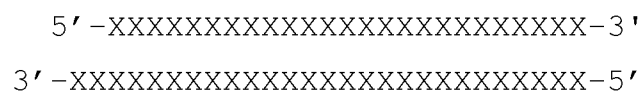
In further embodiments, the DsiRNA comprises:



wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers and underlined residues are 2'-O-methyl RNA monomers. The top strand is the sense strand, and the bottom strand is the antisense strand. In one related embodiment, the DsiRNA comprises:

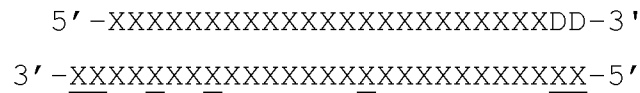


wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers, underlined residues are 2'-O-methyl RNA monomers, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In another related embodiment, the DsiRNA comprises:



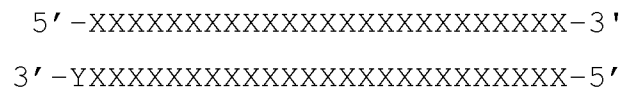
wherein "X"=RNA and "X"=2'-O-methyl RNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In a further related embodiment, the DsiRNA

comprises:

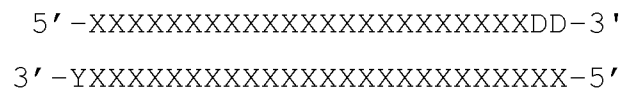


wherein "X"=RNA, "X"=2'-O-methyl RNA, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. This modification pattern is also referred to herein as the "AS-M18" or "M18" modification pattern.

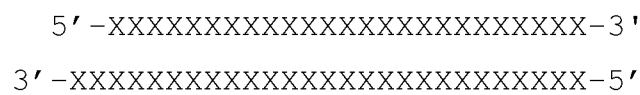
In additional embodiments, the DsiRNA comprises:



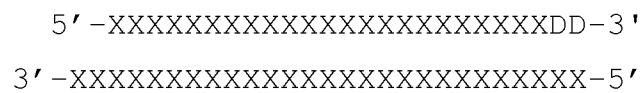
wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers and underlined residues are 2'-O-methyl RNA monomers. The top strand is the sense strand, and the bottom strand is the antisense strand. In one related embodiment, the DsiRNA comprises:



wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers, underlined residues are 2'-O-methyl RNA monomers, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In another related embodiment, the DsiRNA comprises:

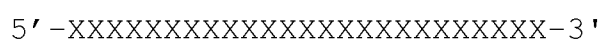


wherein "X"=RNA and "X"=2'-O-methyl RNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In a further related embodiment, the DsiRNA comprises:



wherein "X"=RNA, "X"=2'-O-methyl RNA, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. This modification pattern is also referred to herein as the "AS-M19" or "M19" modification pattern.

In further embodiments, the DsiRNA comprises:



3' - YXXXXXXXXXXXXXXXXXXXXXXXXXXXX - 5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers and underlined residues are 2'-O-methyl RNA monomers. The top strand is the sense strand, and the bottom strand is the antisense strand. In one related embodiment, the DsiRNA comprises:

5' - XXXXXXXXXXXXXXXXXXXXXXXXXXXXDD - 3'

3' - YXXXXXXXXXXXXXXXXXXXXXXXXXXXX - 5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers, underlined residues are 2'-O-methyl RNA monomers, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In another related embodiment, the DsiRNA comprises:

5' - XXXXXXXXXXXXXXXXXXXXXXXXXXXX - 3'

3' - XXXXXXXXXXXXXXXXXXXXXXXXXXXX - 5'

wherein "X"=RNA and "X"=2'-O-methyl RNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In a further related embodiment, the DsiRNA comprises:

5' - XXXXXXXXXXXXXXXXXXXXXXXXXXXXDD - 3'

3' - XXXXXXXXXXXXXXXXXXXXXXXXXXXX - 5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. This modification pattern is also referred to herein as the "AS-M20" or "M20" modification pattern.

In additional embodiments, the DsiRNA comprises:

5' - XXXXXXXXXXXXXXXXXXXXXXXXXXXX - 3'

3' - YXXXXXXXXXXXXXXXXXXXXXXXXXXXX - 5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers and underlined residues are 2'-O-methyl RNA monomers. The top strand is the sense strand, and the bottom strand is the antisense strand. In one related embodiment, the DsiRNA comprises:

5' - XXXXXXXXXXXXXXXXXXXXXXXXXXXXDD - 3'

3' - YXXXXXXXXXXXXXXXXXXXXXXXXXXXX - 5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an overhang domain comprised of 1-4

RNA monomers that are optionally 2'-O-methyl RNA monomers, underlined residues are 2'-O-methyl RNA monomers, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In another related embodiment, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-3'
 3' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA and "X"=2'-O-methyl RNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In a further related embodiment, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXDD-3'
 3' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. This modification pattern is also referred to herein as the "AS-M22" or "M22" modification pattern.

In further embodiments, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-3'
 3' -YXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers and underlined residues are 2'-O-methyl RNA monomers. The top strand is the sense strand, and the bottom strand is the antisense strand. In one related embodiment, the DsiRNA comprises:

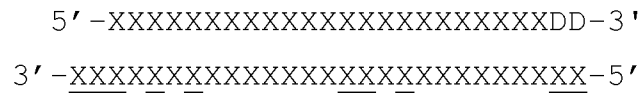
5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXDD-3'
 3' -YXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers, underlined residues are 2'-O-methyl RNA monomers, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In another related embodiment, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-3'
 3' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

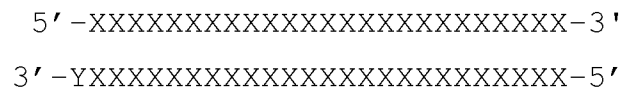
wherein "X"=RNA and "X"=2'-O-methyl RNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In a further related embodiment, the DsiRNA

comprises:

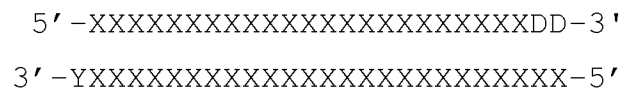


wherein "X"=RNA, "X"=2'-O-methyl RNA, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. This modification pattern is also referred to herein as the "AS-M24" or "M24" modification pattern.

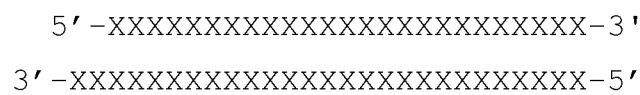
In additional embodiments, the DsiRNA comprises:



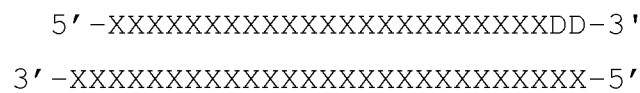
wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers and underlined residues are 2'-O-methyl RNA monomers. The top strand is the sense strand, and the bottom strand is the antisense strand. In one related embodiment, the DsiRNA comprises:



wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers, underlined residues are 2'-O-methyl RNA monomers, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In another related embodiment, the DsiRNA comprises:

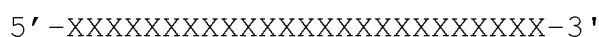


wherein "X"=RNA and "X"=2'-O-methyl RNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In a further related embodiment, the DsiRNA comprises:



wherein "X"=RNA, "X"=2'-O-methyl RNA, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. This modification pattern is also referred to herein as the "AS-M25" or "M25" modification pattern.

In further embodiments, the DsiRNA comprises:



3' - YXXXXXXXXXXXXXXXXXXXXXXXXXXXX - 5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers and underlined residues are 2'-O-methyl RNA monomers. The top strand is the sense strand, and the bottom strand is the antisense strand. In one related embodiment, the DsiRNA comprises:

5' - XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXDD - 3'

3' - YXXXXXXXXXXXXXXXXXXXXXXXXXXXX - 5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers, underlined residues are 2'-O-methyl RNA monomers, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In another related embodiment, the DsiRNA comprises:

5' - XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX - 3'

3' - XXXXXXXXXXXXXXXXXXXXXXXXXXXX - 5'

wherein "X"=RNA and "X"=2'-O-methyl RNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In a further related embodiment, the DsiRNA comprises:

5' - XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXDD - 3'

3' - XXXXXXXXXXXXXXXXXXXXXXXXXXXX - 5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. This modification pattern is also referred to herein as the "AS-M26" or "M26" modification pattern.

In additional embodiments, the DsiRNA comprises:

5' - XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX - 3'

3' - YXXXXXXXXXXXXXXXXXXXXXXXXXXXX - 5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers and underlined residues are 2'-O-methyl RNA monomers. The top strand is the sense strand, and the bottom strand is the antisense strand. In one related embodiment, the DsiRNA comprises:

5' - XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXDD - 3'

3' - YXXXXXXXXXXXXXXXXXXXXXXXXXXXX - 5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an overhang domain comprised of 1-4

RNA monomers that are optionally 2'-O-methyl RNA monomers, underlined residues are 2'-O-methyl RNA monomers, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In another related embodiment, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-3'
 3' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA and "X"=2'-O-methyl RNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In a further related embodiment, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXDD-3'
 3' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. This modification pattern is also referred to herein as the "AS-M27" or "M27" modification pattern.

In further embodiments, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-3'
 3' -YXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers and underlined residues are 2'-O-methyl RNA monomers. The top strand is the sense strand, and the bottom strand is the antisense strand. In one related embodiment, the DsiRNA comprises:

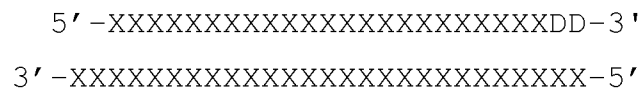
5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXDD-3'
 3' -YXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers, underlined residues are 2'-O-methyl RNA monomers, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In another related embodiment, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-3'
 3' -XXXXXXXXXXXXXXXXXXXXXXXXXX-5'

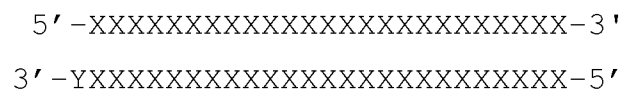
wherein "X"=RNA and "X"=2'-O-methyl RNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In a further related embodiment, the DsiRNA

comprises:

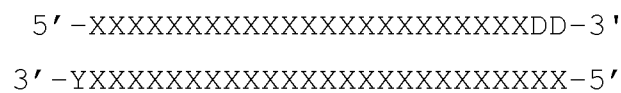


wherein "X"=RNA, "X"=2'-O-methyl RNA, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. This modification pattern is also referred to herein as the "AS-M28" or "M28" modification pattern.

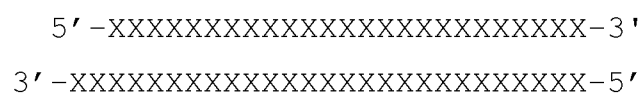
In further embodiments, the DsiRNA comprises:



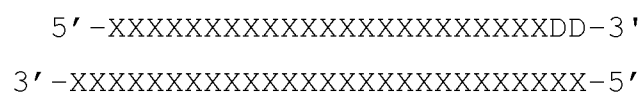
wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers and underlined residues are 2'-O-methyl RNA monomers. The top strand is the sense strand, and the bottom strand is the antisense strand. In one related embodiment, the DsiRNA comprises:



wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers, underlined residues are 2'-O-methyl RNA monomers, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In another related embodiment, the DsiRNA comprises:

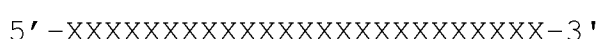


wherein "X"=RNA and "X"=2'-O-methyl RNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In a further related embodiment, the DsiRNA comprises:



wherein "X"=RNA, "X"=2'-O-methyl RNA, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. This modification pattern is also referred to herein as the "AS-M29" or "M29" modification pattern.

In additional embodiments, the DsiRNA comprises:



3' - XXXXXXXXXXXXXXXXXXXXXXXXXXXX - 5'

wherein "X"=RNA and "X"=2'-O-methyl RNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In a further related embodiment, the DsiRNA comprises:

5' - XXXXXXXXXXXXXXXXXXXXXXXXXXXDD - 3'

3' - XXXXXXXXXXXXXXXXXXXXXXXXXXXX - 5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. This modification pattern is also referred to herein as the "AS-M30" or "M30" modification pattern.

In further embodiments, the DsiRNA comprises:

5' - XXXXXXXXXXXXXXXXXXXXXXXXXXX - 3'

3' - XXXXXXXXXXXXXXXXXXXXXXXXXXXX - 5'

wherein "X"=RNA and "X"=2'-O-methyl RNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In a further related embodiment, the DsiRNA comprises:

5' - XXXXXXXXXXXXXXXXXXXXXXXXXXXDD - 3'

3' - XXXXXXXXXXXXXXXXXXXXXXXXXXXX - 5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. This modification pattern is also referred to herein as the "AS-M31" or "M31" modification pattern.

In additional embodiments, the DsiRNA comprises:

5' - XXXXXXXXXXXXXXXXXXXXXXXXXXX - 3'

3' - XXXXXXXXXXXXXXXXXXXXXXXXXXXX - 5'

wherein "X"=RNA and "X"=2'-O-methyl RNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In a further related embodiment, the DsiRNA comprises:

5' - XXXXXXXXXXXXXXXXXXXXXXXXXXXDD - 3'

3' - XXXXXXXXXXXXXXXXXXXXXXXXXXXX - 5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. This modification pattern is also referred to herein as the "AS-M32" or "M32" modification pattern.

In further embodiments, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-3'
 3' -YXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers and underlined residues are 2'-O-methyl RNA monomers. The top strand is the sense strand, and the bottom strand is the antisense strand. In one related embodiment, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXDD-3'
 3' -YXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers, underlined residues are 2'-O-methyl RNA monomers, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In another related embodiment, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-3'
 3' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA and "X"=2'-O-methyl RNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In a further related embodiment, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXDD-3'
 3' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. This modification pattern is also referred to herein as the "AS-M34" or "M34" modification pattern.

In additional embodiments, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-3'
 3' -YXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers and underlined residues are 2'-O-methyl RNA monomers. The top strand is the sense strand, and the bottom strand is the antisense strand. In one related embodiment, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXDD-3'
 3' -YXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an overhang domain comprised of 1-4

RNA monomers that are optionally 2'-O-methyl RNA monomers, underlined residues are 2'-O-methyl RNA monomers, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In another related embodiment, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-3'
 3' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA and "X"=2'-O-methyl RNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In a further related embodiment, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXDD-3'
 3' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. This modification pattern is also referred to herein as the "AS-M35" or "M35" modification pattern.

In further embodiments, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-3'
 3' -YXXXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers and underlined residues are 2'-O-methyl RNA monomers. The top strand is the sense strand, and the bottom strand is the antisense strand. In one related embodiment, the DsiRNA comprises:

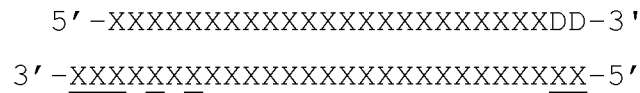
5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXDD-3'
 3' -YXXXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers, underlined residues are 2'-O-methyl RNA monomers, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In another related embodiment, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-3'
 3' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

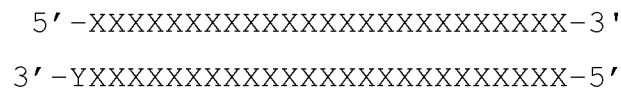
wherein "X"=RNA and "X"=2'-O-methyl RNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In a further related embodiment, the DsiRNA

comprises:

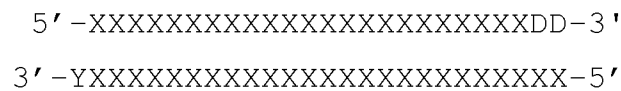


wherein "X"=RNA, "X"=2'-O-methyl RNA, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. This modification pattern is also referred to herein as the "AS-M37" or "M37" modification pattern.

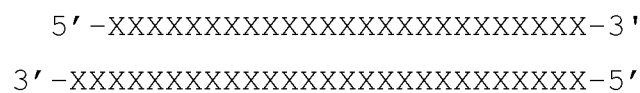
In additional embodiments, the DsiRNA comprises:



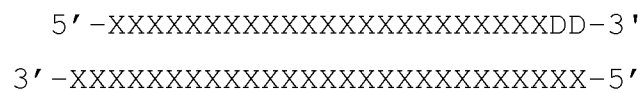
wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers and underlined residues are 2'-O-methyl RNA monomers. The top strand is the sense strand, and the bottom strand is the antisense strand. In one related embodiment, the DsiRNA comprises:



wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers, underlined residues are 2'-O-methyl RNA monomers, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In another related embodiment, the DsiRNA comprises:

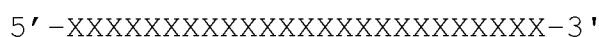


wherein "X"=RNA and "X"=2'-O-methyl RNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In a further related embodiment, the DsiRNA comprises:



wherein "X"=RNA, "X"=2'-O-methyl RNA, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. This modification pattern is also referred to herein as the "AS-M38" or "M38" modification pattern.

In further embodiments, the DsiRNA comprises:



3' - YXXXXXXXXXXXXXXXXXXXXX - 5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers and underlined residues are 2'-O-methyl RNA monomers. The top strand is the sense strand, and the bottom strand is the antisense strand. In one related embodiment, the DsiRNA comprises:

5' - XXXXXXXXXXXXXXXXXXXXXXXDD - 3'

3' - YXXXXXXXXXXXXXXXXXXXXX - 5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers, underlined residues are 2'-O-methyl RNA monomers, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In another related embodiment, the DsiRNA comprises:

5' - XXXXXXXXXXXXXXXXXXXXXXX - 3'

3' - XXXXXXXXXXXXXXXXXXXXX - 5'

wherein "X"=RNA and "X"=2'-O-methyl RNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In a further related embodiment, the DsiRNA comprises:

5' - XXXXXXXXXXXXXXXXXXXXXXXDD - 3'

3' - XXXXXXXXXXXXXXXXXXXXX - 5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. This modification pattern is also referred to herein as the "AS-M40" or "M40" modification pattern.

In additional embodiments, the DsiRNA comprises:

5' - XXXXXXXXXXXXXXXXXXXXXXX - 3'

3' - YXXXXXXXXXXXXXXXXXXXXX - 5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers and underlined residues are 2'-O-methyl RNA monomers. The top strand is the sense strand, and the bottom strand is the antisense strand. In one related embodiment, the DsiRNA comprises:

5' - XXXXXXXXXXXXXXXXXXXXXXXDD - 3'

3' - YXXXXXXXXXXXXXXXXXXXXX - 5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an overhang domain comprised of 1-4

RNA monomers that are optionally 2'-O-methyl RNA monomers, underlined residues are 2'-O-methyl RNA monomers, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In another related embodiment, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-3'
 3' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA and "X"=2'-O-methyl RNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In a further related embodiment, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXDD-3'
 3' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. This modification pattern is also referred to herein as the "AS-M41" or "M41" modification pattern.

In additional embodiments, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-3'
 3' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA and "X"=2'-O-methyl RNA. In a further related embodiment, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXDD-3'
 3' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. This modification pattern is also referred to herein as the "AS-M7*" or "M7*" modification pattern.

In further embodiments, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-3'
 3' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA and "X"=2'-O-methyl RNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In a further related embodiment, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXDD-3'
 3' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. This modification pattern is also referred to herein as the "AS-M6*" or "M6*" modification pattern.

In other embodiments, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-3'
 3' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA and "X"=2'-O-methyl RNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In another related embodiment, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXDD-3'
 3' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. This modification pattern is also referred to herein as the "AS-M5*" or "M5*" modification pattern.

In further embodiments, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-3'
 3' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA and "X"=2'-O-methyl RNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In a further related embodiment, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXDD-3'
 3' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. This modification pattern is also referred to herein as the "AS-M4*" or "M4*" modification pattern.

In additional embodiments, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-3'
 3' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA and "X"=2'-O-methyl RNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In a further related embodiment, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXDD-3'
 3' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. This modification pattern is also referred to herein as the "AS-M8*" or "M8*" modification pattern.

In additional embodiments, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-3'
 3' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA and "X"=2'-O-methyl RNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In a further related embodiment, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXDD-3'
 3' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. This modification pattern is also referred to herein as the "AS-M2*" or "M2*" modification pattern.

In other embodiments, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-3'
 3' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA and "X"=2'-O-methyl RNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In a further related embodiment, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXDD-3'
 3' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. This modification pattern is also referred to herein as the "AS-M10*" or "M10*" modification pattern.

In further embodiments, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-3'
 3' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA and "X"=2'-O-methyl RNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In a further related embodiment, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXDD-3'
 3' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. This modification pattern is also referred to herein as the "AS-M11*" or "M11*" modification pattern.

In further embodiments, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-3'
 3' -XXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA and "X"=2'-O-methyl RNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In a further related embodiment, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXDD-3'
 3' -XXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. This modification pattern is also referred to herein as the "AS-M13*" or "M13*" modification pattern.

In further embodiments, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-3'
 3' -XXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA and "X"=2'-O-methyl RNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In a further related embodiment, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXDD-3'
 3' -XXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. This modification pattern is also referred to herein as the "AS-M14*" or "M14*" modification pattern.

In additional embodiments, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-3'
 3' -XXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA and "X"=2'-O-methyl RNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In a further related embodiment, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXDD-3'
 3' -XXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. This modification pattern is also referred to herein as the "AS-M15*" or "M15*" modification pattern.

In further embodiments, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-3'
 3' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA and "X"=2'-O-methyl RNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In a further related embodiment, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXDD-3'
 3' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. This modification pattern is also referred to herein as the "AS-M16*" or "M16*" modification pattern.

In additional embodiments, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-3'
 3' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA and "X"=2'-O-methyl RNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In a further related embodiment, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXDD-3'
 3' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. This modification pattern is also referred to herein as the "AS-M17*" or "M17*" modification pattern.

In further embodiments, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-3'
 3' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA and "X"=2'-O-methyl RNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In a further related embodiment, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXDD-3'
 3' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. This modification pattern is also referred to herein as the "AS-M18*" or "M18*" modification pattern.

In additional embodiments, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-3'
 3' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA and "X"=2'-O-methyl RNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In a further related embodiment, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXDD-3'
 3' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. This modification pattern is also referred to herein as the "AS-M19*" or "M19*" modification pattern.

In further embodiments, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXDD-3'
 3' -YXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers, underlined residues are 2'-O-methyl RNA monomers, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In another related embodiment, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-3'
 3' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA and "X"=2'-O-methyl RNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In a further related embodiment, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXDD-3'
 3' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. This modification pattern is also referred to herein as the "AS-M20*" or "M20*" modification pattern.

In additional embodiments, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-3'
 3' -XXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA and "X"=2'-O-methyl RNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In a further related embodiment, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXDD-3'
 3' -XXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. This modification pattern is also referred to herein as the "AS-M22*" or "M22*" modification pattern.

In further embodiments, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-3'
 3' -XXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA and "X"=2'-O-methyl RNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In a further related embodiment, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXDD-3'
 3' -XXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. This modification pattern is also referred to herein as the "AS-M24*" or "M24*" modification pattern.

In additional embodiments, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-3'
 3' -XXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA and "X"=2'-O-methyl RNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In a further related embodiment, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXDD-3'
 3' -XXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. This modification pattern is also referred to herein as the "AS-M25*" or "M25*" modification pattern.

In further embodiments, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-3'
 3' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA and "X"=2'-O-methyl RNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In a further related embodiment, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXDD-3'
 3' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. This modification pattern is also referred to herein as the "AS-M26*" or "M26*" modification pattern.

In additional embodiments, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-3'
 3' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA and "X"=2'-O-methyl RNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In a further related embodiment, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXDD-3'
 3' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. This modification pattern is also referred to herein as the "AS-M27*" or "M27*" modification pattern.

In additional embodiments, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-3'
 3' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA and "X"=2'-O-methyl RNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In a further related embodiment, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXDD-3'
 3' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. This modification pattern is also referred to herein as the "AS-M28*" or "M28*" modification pattern.

In further embodiments, the DsiRNA comprises:

$5' - \text{XXXXXXXXXXXXXXXXXXXXXXXXXXXX} - 3'$

$3' - \text{XXXXXXXXXXXXXXXXXXXXXXXXXXXX} - 5'$

wherein "X"=RNA and "X"=2'-O-methyl RNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In a further related embodiment, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXDD-3'
3' -XXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. This modification pattern is also referred to herein as the "AS-M29*" or "M29*" modification pattern.

In additional embodiments, the DsiRNA comprises:

[illegible]

wherein "X"=RNA and "X"=2'-O-methyl RNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In a further related embodiment, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXDD-3'
3' -XXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. This modification pattern is also referred to herein as the "AS-M34*" or "M34*" modification pattern.

In further embodiments, the DsiRNA comprises:

[illegible]

wherein "X"=RNA and "X"=2'-O-methyl RNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In a further related embodiment, the DsiRNA comprises:

5'-XXXXXXXXXXXXXXXXXXXXDD-3'
3'-XXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. This modification pattern is also referred to herein as the "AS-M35*" or "M35*" modification pattern.

In additional embodiments, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-3'
 3' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA and "X"=2'-O-methyl RNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In a further related embodiment, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXDD-3'
 3' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. This modification pattern is also referred to herein as the "AS-M37*" or "M37*" modification pattern.

In further embodiments, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-3'
 3' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA and "X"=2'-O-methyl RNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In a further related embodiment, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXDD-3'
 3' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. This modification pattern is also referred to herein as the "AS-M38*" or "M38*" modification pattern.

In further embodiments, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-3'
 3' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA and "X"=2'-O-methyl RNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In a further related embodiment, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXDD-3'
 3' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. This modification pattern is also referred to herein as the "AS-M40*" or "M40*" modification pattern.

In additional embodiments, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-3'
 3' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA and "X"=2'-O-methyl RNA. The top strand is the sense strand, and the bottom strand is the antisense strand. In a further related embodiment, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXDD-3'
 3' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, and "D"=DNA. The top strand is the sense strand, and the bottom strand is the antisense strand. This modification pattern is also referred to herein as the "AS-M41*" or "M41*" modification pattern.

In certain embodiments, the sense strand of a DsiRNA of the invention is modified – specific exemplary forms of sense strand modifications are shown below, and it is contemplated that such modified sense strands can be substituted for the sense strand of any of the DsiRNAs shown above to generate a DsiRNA comprising a below-depicted sense strand that anneals with an above-depicted antisense strand. Exemplary sense strand modification patterns include:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXDD-3' "SM1"
 5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXDD-3' "SM2"
 5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXDD-3' "SM3"
 5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXDD-3' "SM4"
 5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXDD-3' "SM5"
 5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXDD-3' "SM6"
 5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXDD-3' "SM7"
 5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXDD-3' "SM8"
 5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXDD-3' "SM9"
 5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXDD-3' "SM10"
 5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXDD-3' "SM11"
 5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXDD-3' "SM12"
 5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXDD-3' "SM13"
 5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXDD-3' "SM14"
 5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXDD-3' "SM15"
 5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXXDD-3' "SM16"
 5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-3'
 5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-3'
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 5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-3'
 5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX-3'

where "X"=RNA, "X"=2'-O-methyl RNA, and "D"=DNA.

The above modification patterns can also be incorporated into, *e.g.*, the extended DsiRNA structures and mismatch and/or frayed DsiRNA structures described below.

In another embodiment, the DsiRNA comprises strands having equal lengths possessing 1-3 mismatched residues that serve to orient Dicer cleavage (specifically, one or more of positions 1, 2 or 3 on the first strand of the DsiRNA, when numbering from the 3'-terminal residue, are mismatched with corresponding residues of the 5'-terminal region on the second strand when first and second strands are annealed to one another). An exemplary 27mer DsiRNA agent with two terminal mismatched residues is shown:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX^M-3'
 3' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX_M-5'

wherein "X"=RNA, "M"=Nucleic acid residues (RNA, DNA or non-natural or modified nucleic acids) that do not base pair (hydrogen bond) with corresponding "M" residues of otherwise complementary strand when strands are annealed. Any of the residues of such agents can optionally be 2'-O-methyl RNA monomers – alternating positioning of 2'-O-methyl RNA monomers that commences from the 3'-terminal residue of the bottom (second) strand, as shown for above asymmetric agents, can also be used in the above "blunt/fray" DsiRNA agent. In one embodiment, the top strand is the sense strand, and the bottom strand is the antisense strand. Alternatively, the bottom strand is the sense strand and the top strand is the antisense strand.

In certain additional embodiments, the present invention provides compositions for RNA interference (RNAi) that possess one or more base paired deoxyribonucleotides within a region of a double stranded ribonucleic acid (dsRNA) that is positioned 3' of a projected sense strand Dicer cleavage site and correspondingly 5' of a projected antisense strand Dicer cleavage site. The compositions of the invention comprise a dsRNA which is a precursor molecule, *i.e.*, the dsRNA of the present invention is processed *in vivo* to produce an active

small interfering nucleic acid (siRNA). The dsRNA is processed by Dicer to an active siRNA which is incorporated into RISC.

In certain embodiments, the DsiRNA agents of the invention can have the following exemplary structures (noting that any of the following exemplary structures can be combined, *e.g.*, with the bottom strand modification patterns of the above-described structures – in one specific example, the bottom strand modification pattern shown in any of the above structures is applied to the 27 most 3' residues of the bottom strand of any of the following structures; in another specific example, the bottom strand modification pattern shown in any of the above structures upon the 23 most 3' residues of the bottom strand is applied to the 23 most 3' residues of the bottom strand of any of the following structures):

In one such embodiment, the DsiRNA comprises the following (an exemplary “right-extended”, “DNA extended” DsiRNA):

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX_N*D_NDD-3'

3' -YXXXXXXXXXXXXXXXXXXXXXXXXXXXX_N*D_NXX-5'

wherein “X”=RNA, “Y” is an optional overhang domain comprised of 0-10 RNA monomers that are optionally 2'-O-methyl RNA monomers – in certain embodiments, “Y” is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers, “D”=DNA, and “N”=1 to 50 or more, but is optionally 1-8 or 1-10. “N*”=0 to 15 or more, but is optionally 0, 1, 2, 3, 4, 5 or 6. In one embodiment, the top strand is the sense strand, and the bottom strand is the antisense strand. Alternatively, the bottom strand is the sense strand and the top strand is the antisense strand.

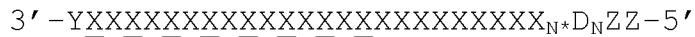
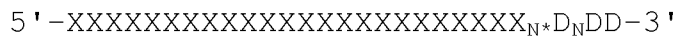
In a related embodiment, the DsiRNA comprises:

5' -XXXXXXXXXXXXXXXXXXXXXXXXXXXX_N*D_NDD-3'

3' -YXXXXXXXXXXXXXXXXXXXXXXXXXXXX_N*D_NDD-5'

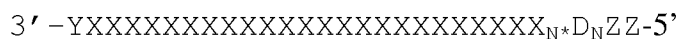
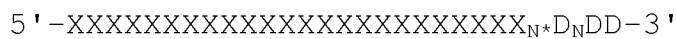
wherein “X”=RNA, “Y” is an optional overhang domain comprised of 0-10 RNA monomers that are optionally 2'-O-methyl RNA monomers – in certain embodiments, “Y” is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers, “D”=DNA, and “N”=1 to 50 or more, but is optionally 1-8 or 1-10. “N*”=0 to 15 or more, but is optionally 0, 1, 2, 3, 4, 5 or 6. In one embodiment, the top strand is the sense strand, and the bottom strand is the antisense strand. Alternatively, the bottom strand is the sense strand and the top strand is the antisense strand.

In an additional embodiment, the DsiRNA comprises:



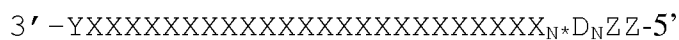
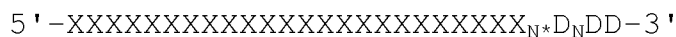
wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an optional overhang domain comprised of 0-10 RNA monomers that are optionally 2'-O-methyl RNA monomers – in certain embodiments, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers, "D"=DNA, "Z"=DNA or RNA, and "N"=1 to 50 or more, but is optionally 1-8 or 1-10. "N*" = 0 to 15 or more, but is optionally 0, 1, 2, 3, 4, 5 or 6. In one embodiment, the top strand is the sense strand, and the bottom strand is the antisense strand. Alternatively, the bottom strand is the sense strand and the top strand is the antisense strand, with 2'-O-methyl RNA monomers located at alternating residues along the top strand, rather than the bottom strand presently depicted in the above schematic.

In another such embodiment, the DsiRNA comprises:



wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an optional overhang domain comprised of 0-10 RNA monomers that are optionally 2'-O-methyl RNA monomers – in certain embodiments, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers, "D"=DNA, "Z"=DNA or RNA, and "N"=1 to 50 or more, but is optionally 1-8 or 1-10. "N*" = 0 to 15 or more, but is optionally 0, 1, 2, 3, 4, 5 or 6. In one embodiment, the top strand is the sense strand, and the bottom strand is the antisense strand. Alternatively, the bottom strand is the sense strand and the top strand is the antisense strand, with 2'-O-methyl RNA monomers located at alternating residues along the top strand, rather than the bottom strand presently depicted in the above schematic.

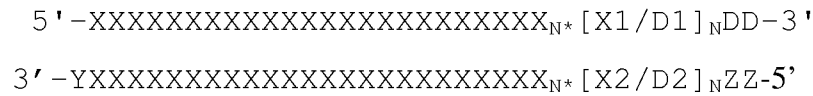
In another such embodiment, the DsiRNA comprises:



wherein "X"=RNA, "X"=2'-O-methyl RNA, "Y" is an optional overhang domain comprised of 0-10 RNA monomers that are optionally 2'-O-methyl RNA monomers – in certain embodiments, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers, "D"=DNA, "Z"=DNA or RNA, and "N"=1 to 50 or more, but is optionally 1-8 or 1-10. "N*" = 0 to 15 or more, but is optionally 0, 1, 2, 3, 4, 5 or 6. In one embodiment, the top strand is the sense strand, and the bottom strand is the

antisense strand. Alternatively, the bottom strand is the sense strand and the top strand is the antisense strand, with 2'-O-methyl RNA monomers located at alternating residues along the top strand, rather than the bottom strand presently depicted in the above schematic.

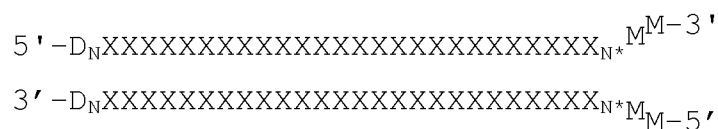
In another embodiment, the DsiRNA comprises:



wherein "X"=RNA, "Y" is an optional overhang domain comprised of 0-10 RNA monomers that are optionally 2'-O-methyl RNA monomers – in certain embodiments, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers, "D"=DNA, "Z"=DNA or RNA, and "N"=1 to 50 or more, but is optionally 1-8 or 1-10, where at least one D1_N is present in the top strand and is base paired with a corresponding D2_N in the bottom strand. Optionally, D1_N and D1_{N+1} are base paired with corresponding D2_N and D2_{N+1}; D1_N, D1_{N+1} and D1_{N+2} are base paired with corresponding D2_N, D1_{N+1} and D1_{N+2}, etc. "N*" = 0 to 15 or more, but is optionally 0, 1, 2, 3, 4, 5 or 6. In one embodiment, the top strand is the sense strand, and the bottom strand is the antisense strand. Alternatively, the bottom strand is the sense strand and the top strand is the antisense strand, with 2'-O-methyl RNA monomers located at alternating residues along the top strand, rather than the bottom strand presently depicted in the above schematic.

In the structures depicted herein, the 5' end of either the sense strand or antisense strand can optionally comprise a phosphate group.

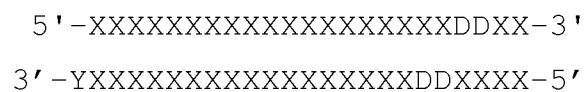
In another embodiment, a DNA:DNA-extended DsiRNA comprises strands having equal lengths possessing 1-3 mismatched residues that serve to orient Dicer cleavage (specifically, one or more of positions 1, 2 or 3 on the first strand of the DsiRNA, when numbering from the 3'-terminal residue, are mismatched with corresponding residues of the 5'-terminal region on the second strand when first and second strands are annealed to one another). An exemplary DNA:DNA-extended DsiRNA agent with two terminal mismatched residues is shown:



wherein "X"=RNA, "M"=Nucleic acid residues (RNA, DNA or non-natural or modified nucleic acids) that do not base pair (hydrogen bond) with corresponding "M" residues of otherwise complementary strand when strands are annealed, "D"=DNA and "N"=1 to 50 or

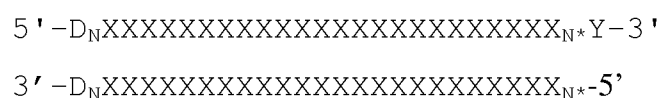
more, but is optionally 1-15 or, optionally, 1-8. "N*" = 0 to 15 or more, but is optionally 0, 1, 2, 3, 4, 5 or 6. Any of the residues of such agents can optionally be 2'-O-methyl RNA monomers – alternating positioning of 2'-O-methyl RNA monomers that commences from the 3'-terminal residue of the bottom (second) strand, as shown for above asymmetric agents, can also be used in the above "blunt/fray" DsiRNA agent. In one embodiment, the top strand (first strand) is the sense strand, and the bottom strand (second strand) is the antisense strand. Alternatively, the bottom strand is the sense strand and the top strand is the antisense strand. Modification and DNA:DNA extension patterns paralleling those shown above for asymmetric/overhang agents can also be incorporated into such "blunt/frayed" agents.

In one embodiment, a length-extended DsiRNA agent is provided that comprises deoxyribonucleotides positioned at sites modeled to function *via* specific direction of Dicer cleavage, yet which does not require the presence of a base-paired deoxyribonucleotide in the dsRNA structure. An exemplary structure for such a molecule is shown:



wherein "X" = RNA, "Y" is an optional overhang domain comprised of 0-10 RNA monomers that are optionally 2'-O-methyl RNA monomers – in certain embodiments, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers, and "D" = DNA. In one embodiment, the top strand is the sense strand, and the bottom strand is the antisense strand. Alternatively, the bottom strand is the sense strand and the top strand is the antisense strand. The above structure is modeled to force Dicer to cleave a minimum of a 21mer duplex as its primary post-processing form. In embodiments where the bottom strand of the above structure is the antisense strand, the positioning of two deoxyribonucleotide residues at the ultimate and penultimate residues of the 5' end of the antisense strand will help reduce off-target effects (as prior studies have shown a 2'-O-methyl modification of at least the penultimate position from the 5' terminus of the antisense strand to reduce off-target effects; see, *e.g.*, US 2007/0223427).

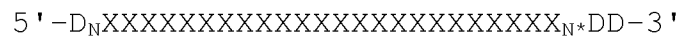
In one embodiment, the DsiRNA comprises the following (an exemplary "left-extended", "DNA extended" DsiRNA):



wherein "X" = RNA, "Y" is an optional overhang domain comprised of 0-10 RNA monomers

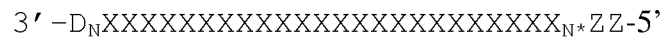
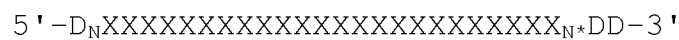
that are optionally 2'-O-methyl RNA monomers – in certain embodiments, “Y” is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers, “D”=DNA, and “N”=1 to 50 or more, but is optionally 1-8 or 1-10. “N*”=0 to 15 or more, but is optionally 0, 1, 2, 3, 4, 5 or 6. In one embodiment, the top strand is the sense strand, and the bottom strand is the antisense strand. Alternatively, the bottom strand is the sense strand and the top strand is the antisense strand.

In a related embodiment, the DsiRNA comprises:



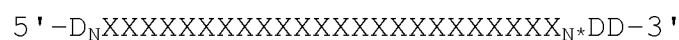
wherein "X"=RNA, optionally a 2'-O-methyl RNA monomers "D"=DNA, "N"=1 to 50 or more, but is optionally 1-8 or 1-10. "N*" = 0 to 15 or more, but is optionally 0, 1, 2, 3, 4, 5 or 6. In one embodiment, the top strand is the sense strand, and the bottom strand is the antisense strand. Alternatively, the bottom strand is the sense strand and the top strand is the antisense strand.

In an additional embodiment, the DsiRNA comprises:



wherein "X"=RNA, optionally a 2'-O-methyl RNA monomers "D"=DNA, "N"=1 to 50 or more, but is optionally 1-8 or 1-10. "N*" = 0 to 15 or more, but is optionally 0, 1, 2, 3, 4, 5 or 6. "Z"=DNA or RNA. In one embodiment, the top strand is the sense strand, and the bottom strand is the antisense strand. Alternatively, the bottom strand is the sense strand and the top strand is the antisense strand, with 2'-O-methyl RNA monomers located at alternating residues along the top strand, rather than the bottom strand presently depicted in the above schematic.

In another such embodiment, the DsiRNA comprises:



wherein "X"=RNA, optionally a 2'-O-methyl RNA monomers "D"=DNA, "N"=1 to 50 or more, but is optionally 1-8 or 1-10. "N*" =0 to 15 or more, but is optionally 0, 1, 2, 3, 4, 5 or 6. "Z"=DNA or RNA. In one embodiment, the top strand is the sense strand, and the bottom strand is the antisense strand. Alternatively, the bottom strand is the sense strand and the top strand is the antisense strand, with 2'-O-methyl RNA monomers located at alternating

residues along the top strand, rather than the bottom strand presently depicted in the above schematic.

In another such embodiment, the DsiRNA comprises:

5' -D_NZXXXXXXXXXXXXXXXXXXXXXXXXXXXXX_N*DD-3'

3' -D_NXXXXXXXXXXXXXXXXXXXXXXXXXXXXX_N*Z-5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, "D"=DNA, "Z"=DNA or RNA, and "N"=1 to 50 or more, but is optionally 1-8 or 1-10. "N*" = 0 to 15 or more, but is optionally 0, 1, 2, 3, 4, 5 or 6. In one embodiment, the top strand is the sense strand, and the bottom strand is the antisense strand. Alternatively, the bottom strand is the sense strand and the top strand is the antisense strand, with 2'-O-methyl RNA monomers located at alternating residues along the top strand, rather than the bottom strand presently depicted in the above schematic.

In another such embodiment, the DsiRNA comprises:

5' -D_NZXXXXXXXXXXXXXXXXXXXXXXXXXXXXX_N*Y-3'

3' -D_NXXXXXXXXXXXXXXXXXXXXXXXXXXXXX_N*-5'

wherein "X"=RNA, "X"=2'-O-methyl RNA, "D"=DNA, "Z"=DNA or RNA, and "N"=1 to 50 or more, but is optionally 1-8 or 1-10. "N*" = 0 to 15 or more, but is optionally 0, 1, 2, 3, 4, 5 or 6. "Y" is an optional overhang domain comprised of 0-10 RNA monomers that are optionally 2'-O-methyl RNA monomers – in certain embodiments, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers. In one embodiment, the top strand is the sense strand, and the bottom strand is the antisense strand. Alternatively, the bottom strand is the sense strand and the top strand is the antisense strand, with 2'-O-methyl RNA monomers located at alternating residues along the top strand, rather than the bottom strand presently depicted in the above schematic.

In another embodiment, the DsiRNA comprises:

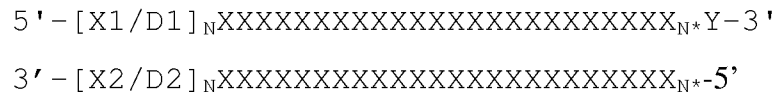
5' - [X₁/D₁]_NXXXXXXXXXXXXXXXXXXXXXXXXXXXXX_N*DD-3'

3' - [X₂/D₂]_NXXXXXXXXXXXXXXXXXXXXXXXXXXXXX_N*ZZ-5'

wherein "X"=RNA, "D"=DNA, "Z"=DNA or RNA, and "N"=1 to 50 or more, but is optionally 1-8 or 1-10, where at least one D_{1N} is present in the top strand and is base paired with a corresponding D_{2N} in the bottom strand. Optionally, D_{1N} and D_{1N+1} are base paired with corresponding D_{2N} and D_{2N+1}; D_{1N}, D_{1N+1} and D_{1N+2} are base paired with corresponding D_{2N}, D_{1N+1} and D_{1N+2}, etc. "N*" = 0 to 15 or more, but is optionally 0, 1, 2, 3, 4, 5 or 6. In one embodiment, the top strand is the sense strand, and the bottom strand is the

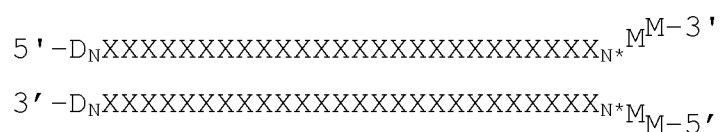
antisense strand. Alternatively, the bottom strand is the sense strand and the top strand is the antisense strand, with 2'-O-methyl RNA monomers located at alternating residues along the top strand, rather than the bottom strand presently depicted in the above schematic.

In a related embodiment, the DsiRNA comprises:



wherein "X"=RNA, "D"=DNA, "Y" is an optional overhang domain comprised of 0-10 RNA monomers that are optionally 2'-O-methyl RNA monomers – in certain embodiments, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers, and "N"=1 to 50 or more, but is optionally 1-8 or 1-10, where at least one D1_N is present in the top strand and is base paired with a corresponding D2_N in the bottom strand. Optionally, D1_N and D1_{N+1} are base paired with corresponding D2_N and D2_{N+1}; D1_N, D1_{N+1} and D1_{N+2} are base paired with corresponding D2_N, D1_{N+1} and D1_{N+2}, etc. "N*" = 0 to 15 or more, but is optionally 0, 1, 2, 3, 4, 5 or 6. In one embodiment, the top strand is the sense strand, and the bottom strand is the antisense strand. Alternatively, the bottom strand is the sense strand and the top strand is the antisense strand, with 2'-O-methyl RNA monomers located at alternating residues along the top strand, rather than the bottom strand presently depicted in the above schematic.

In another embodiment, the DNA:DNA-extended DsiRNA comprises strands having equal lengths possessing 1-3 mismatched residues that serve to orient Dicer cleavage (specifically, one or more of positions 1, 2 or 3 on the first strand of the DsiRNA, when numbering from the 3'-terminal residue, are mismatched with corresponding residues of the 5'-terminal region on the second strand when first and second strands are annealed to one another). An exemplary DNA:DNA-extended DsiRNA agent with two terminal mismatched residues is shown:



wherein "X"=RNA, "M"=Nucleic acid residues (RNA, DNA or non-natural or modified nucleic acids) that do not base pair (hydrogen bond) with corresponding "M" residues of otherwise complementary strand when strands are annealed, "D"=DNA and "N"=1 to 50 or more, but is optionally 1-8 or 1-10. "N*" = 0 to 15 or more, but is optionally 0, 1, 2, 3, 4, 5 or 6. Any of the residues of such agents can optionally be 2'-O-methyl RNA monomers –

alternating positioning of 2'-O-methyl RNA monomers that commences from the 3'-terminal residue of the bottom (second) strand, as shown for above asymmetric agents, can also be used in the above "blunt/fray" DsiRNA agent. In one embodiment, the top strand (first strand) is the sense strand, and the bottom strand (second strand) is the antisense strand. Alternatively, the bottom strand is the sense strand and the top strand is the antisense strand. Modification and DNA:DNA extension patterns paralleling those shown above for asymmetric/overhang agents can also be incorporated into such "blunt/frayed" agents.

In another embodiment, a length-extended DsiRNA agent is provided that comprises deoxyribonucleotides positioned at sites modeled to function *via* specific direction of Dicer cleavage, yet which does not require the presence of a base-paired deoxyribonucleotide in the dsRNA structure. Exemplary structures for such a molecule are shown:

5' -XXDDXXXXXXXXXXXXXXXXXXXXX_{N*}Y-3'

3' -DDXXXXXXXXXXXXXXXXXXXXX_{N*}-5'

or

5' -XDXDXXXXXXXXXXXXXXXXXXXXX_{N*}Y-3'

3' -DXDXXXXXXXXXXXXXXXXXXXXX_{N*}-5'

wherein "X"=RNA, "Y" is an optional overhang domain comprised of 0-10 RNA monomers that are optionally 2'-O-methyl RNA monomers – in certain embodiments, "Y" is an overhang domain comprised of 1-4 RNA monomers that are optionally 2'-O-methyl RNA monomers, and "D"=DNA. "N*" = 0 to 15 or more, but is optionally 0, 1, 2, 3, 4, 5 or 6. In one embodiment, the top strand is the sense strand, and the bottom strand is the antisense strand. Alternatively, the bottom strand is the sense strand and the top strand is the antisense strand.

In any of the above embodiments where the bottom strand of the above structure is the antisense strand, the positioning of two deoxyribonucleotide residues at the ultimate and penultimate residues of the 5' end of the antisense strand will help reduce off-target effects (as prior studies have shown a 2'-O-methyl modification of at least the penultimate position from the 5' terminus of the antisense strand to reduce off-target effects; see, *e.g.*, US 2007/0223427).

In certain embodiments, the "D" residues of the above structures include at least one PS-DNA or PS-RNA. Optionally, the "D" residues of the above structures include at least one modified nucleotide that inhibits Dicer cleavage.

While the above-described “DNA-extended” DsiRNA agents can be categorized as either “left extended” or “right extended”, DsiRNA agents comprising both left- and right-extended DNA-containing sequences within a single agent (*e.g.*, both flanks surrounding a core dsRNA structure are dsDNA extensions) can also be generated and used in similar manner to those described herein for “right-extended” and “left-extended” agents.

In some embodiments, the DsiRNA of the instant invention further comprises a linking moiety or domain that joins the sense and antisense strands of a DNA:DNA-extended DsiRNA agent. Optionally, such a linking moiety domain joins the 3' end of the sense strand and the 5' end of the antisense strand. The linking moiety may be a chemical (non-nucleotide) linker, such as an oligomethylenediol linker, oligoethylene glycol linker, or other art-recognized linker moiety. Alternatively, the linker can be a nucleotide linker, optionally including an extended loop and/or tetraloop.

In one embodiment, the DsiRNA agent has an asymmetric structure, with the sense strand having a 25-base pair length, and the antisense strand having a 27-base pair length with a 1-4 base 3'-overhang (*e.g.*, a one base 3'-overhang, a two base 3'-overhang, a three base 3'-overhang or a four base 3'-overhang). In another embodiment, this DsiRNA agent has an asymmetric structure further containing 2 deoxynucleotides at the 3' end of the sense strand.

In another embodiment, the DsiRNA agent has an asymmetric structure, with the antisense strand having a 25-base pair length, and the sense strand having a 27-base pair length with a 1-4 base 3'-overhang (*e.g.*, a one base 3'-overhang, a two base 3'-overhang, a three base 3'-overhang or a four base 3'-overhang). In another embodiment, this DsiRNA agent has an asymmetric structure further containing 2 deoxyribonucleotides at the 3' end of the antisense strand.

Exemplary EGFR targeting DsiRNA agents of the invention, and their associated EGFR target sequences, include the following, presented in the below series of tables:

Table Number:

- (2) Selected Human Anti-EGFR DsiRNA Agents (Asymmetries);
- (3) Selected Human Anti-EGFR DsiRNAs, Unmodified Duplexes (Asymmetries);
- (4) Selected Mouse Anti-EGFR DsiRNAs (Asymmetries);
- (5) Selected Mouse Anti-EGFR DsiRNAs, Unmodified Duplexes (Asymmetries);
- (6) DsiRNA Target Sequences (21mers) in EGFR;

- (7) Selected Human Anti-EGFR “Blunt/Fray” DsiRNAs;
- (8) Selected Mouse Anti-EGFR “Blunt/Fray” DsiRNAs;
- (9) Selected Human Anti-EGFR “Blunt/Blunt” DsiRNAs; and
- (10) Selected Mouse Anti-EGFR “Blunt/Blunt” DsiRNAs.

Table 2: Selected Human Anti-EGFR DsiRNA Agents (Asymmetrics)

5'-CGCAGCGCGGCCGCGAGCAGCCUCgc-3' (SEQ ID NO: 1)
3'- <u>CCGCGUCGCGCCGGCGUCGUCGAGGC</u> -5' (SEQ ID NO: 357)
EGFR-31 Target: 5'-GGCGCAGCGCGGCCGCGAGCAGCCTCCG-3' (SEQ ID NO: 713)
5'-GCAGCGCGGCCGCGAGCAGCCUCCgc-3' (SEQ ID NO: 2)
3'- <u>CGCGUCGCGCCGGCGUCGUCGAGGCG</u> -5' (SEQ ID NO: 358)
EGFR-32 Target: 5'-GCGCAGCGCGGCCGCGAGCAGCCTCCGC-3' (SEQ ID NO: 714)
5'-AGCGCGGCCGCGAGCAGCCUCCGCcc-3' (SEQ ID NO: 3)
3'- <u>CGUCGCGCGCCGGCGUCGUCGAGGCGGG</u> -5' (SEQ ID NO: 359)
EGFR-34 Target: 5'-GCAGCGCGGCCGCGAGCAGCCTCCGCC-3' (SEQ ID NO: 715)
5'-GCGCUCCUGGCGCUGCUGGCUGCgc-3' (SEQ ID NO: 4)
3'- <u>GUCGCGAGGACCGCGACGACCGACGCG</u> -5' (SEQ ID NO: 360)
EGFR-298 Target: 5'-CAGCGCTCCTGGCGCTGCTGGCTGCGC-3' (SEQ ID NO: 716)
5'-GCUCCUGGCGCUGCUGGCUGCGCtc-3' (SEQ ID NO: 5)
3'- <u>CGCGAGGACCGCGACGACCGACGCGAG</u> -5' (SEQ ID NO: 361)
EGFR-300 Target: 5'-GCGCTCCTGGCGCTGCTGGCTGCGCTC-3' (SEQ ID NO: 717)
5'-UCCUGGCGCUGCUGGCUGCGCUCtg-3' (SEQ ID NO: 6)
3'- <u>CGAGGACCGCGACGACCGACGCGAGAC</u> -5' (SEQ ID NO: 362)
EGFR-302 Target: 5'-GCTCCTGGCGCTGCTGGCTGCGCTCTG-3' (SEQ ID NO: 718)
5'-GUUGGGCACUUUUGAAGAUCAUUt-3' (SEQ ID NO: 7)
3'- <u>GUCAACCCGUGAAAACUUCUAGUAAAA</u> -5' (SEQ ID NO: 363)
EGFR-390 Target: 5'-CAGTTGGGCACTTTTGAAGATCATTTT-3' (SEQ ID NO: 719)
5'-GGAAUUUGGAAAUUACCUAUGUGca-3' (SEQ ID NO: 8)
3'- <u>ACCCUAAAACCUUUAUUGGAUACACGU</u> -5' (SEQ ID NO: 364)
EGFR-458 Target: 5'-TGGGAATTTGGAAATTACCTATGTGCA-3' (SEQ ID NO: 720)
5'-UUAUGAUCUUCCUUCUUAAGAcc-3' (SEQ ID NO: 9)
3'- <u>UUAUACUAGAAAGGAAGAAUUCUGG</u> -5' (SEQ ID NO: 365)
EGFR-489 Target: 5'-AATTATGATCTTTCCTTCTAAAGACC-3' (SEQ ID NO: 721)
5'-GGCUGGUUAUGUCCUCAUUGCCctc-3' (SEQ ID NO: 10)
3'- <u>CACCGACCAUACAGGAGUAACGGGAG</u> -5' (SEQ ID NO: 366)

EGFR-525 Target: 5'-GTGGCTGGTTATGTCTCATTTGCCCTC-3' (SEQ ID NO: 722)

5'-CCCAUGAGAAAUUUACAGGAAAUcc-3' (SEQ ID NO: 11)
3'-ACGGGUACUCUUUAAAUGUCCUUUAGG-5' (SEQ ID NO: 367)

EGFR-676 Target: 5'-TGCCCATGAGAAATTTACAGGAAATCC-3' (SEQ ID NO: 723)

5'-UGCAUGGCGCCGUGCGGUUCAGCaa-3' (SEQ ID NO: 12)
3'-GGACGUACCGCGGCACGCCAAGUCGUU-5' (SEQ ID NO: 368)

EGFR-701 Target: 5'-CCTGCATGGCGCCGTGCGGTTTACAGCA-3' (SEQ ID NO: 724)

5'-GCGCCGUGCGGUUCAGCAACAACcc-3' (SEQ ID NO: 13)
3'-ACCGCGGCCACGCCAAGUCGUUGUUGGG-5' (SEQ ID NO: 369)

EGFR-707 Target: 5'-TGGCGCCGTGCGGTTTACAGCAACAACCC-3' (SEQ ID NO: 725)

5'-GCGCCGUGCGGUUCAGCAACAACcc-3' (SEQ ID NO: 14)
3'-ACCGCGGCCACGCCAAGUCGUUGUUGGG-5' (SEQ ID NO: 370)

EGFR-707 Target: 5'-TGGCGCCGTGCGGTTTACAGCAACAACCC-3' (SEQ ID NO: 726)

5'-GCCGUGCGGUUCAGCAACAACCCtg-3' (SEQ ID NO: 15)
3'-CGCGGCCACGCCAAGUCGUUGUUGGGAC-5' (SEQ ID NO: 371)

EGFR-709 Target: 5'-GCGCCGTGCGGTTTACAGCAACAACCCCTG-3' (SEQ ID NO: 727)

5'-CCGUGCGGUUCAGCAACAACCCUgc-3' (SEQ ID NO: 16)
3'-GCGGCCACGCCAAGUCGUUGUUGGGACG-5' (SEQ ID NO: 372)

EGFR-710 Target: 5'-CGCCGTGCGGTTTACAGCAACAACCCCTGC-3' (SEQ ID NO: 728)

5'-GCUGCCAAAAGUGUGAUCCAAGCtg-3' (SEQ ID NO: 17)
3'-GUCGACCGGUUUUCACACUAGGUUCGAC-5' (SEQ ID NO: 373)

EGFR-827 Target: 5'-CAGCTGCCAAAAGTGTGATCCAAGCTG-3' (SEQ ID NO: 729)

5'-CUGUGCCCAGCAGUGCUCCGGGCgc-3' (SEQ ID NO: 18)
3'-UAGACACGGGUCGUCACGAGGCCCGCG-5' (SEQ ID NO: 374)

EGFR-912 Target: 5'-ATCTGTGCCCAGCAGTGCTCCGGGCGC-3' (SEQ ID NO: 730)

5'-GUGCCCAGCAGUGCUCCGGGCGtg-3' (SEQ ID NO: 19)
3'-GACACGGGUCGUCACGAGGCCCGCGAC-5' (SEQ ID NO: 375)

EGFR-914 Target: 5'-CTGTGCCCAGCAGTGCTCCGGGCGCTG-3' (SEQ ID NO: 731)

5'-GCUCCGGGCGCUGCCGUGGCAAGtc-3' (SEQ ID NO: 20)
3'-CACGAGGCCCGCGACGGCACCGUUCAG-5' (SEQ ID NO: 376)

EGFR-926 Target: 5'-GTGCTCCGGGCGCTGCCGTGGCAAGTC-3' (SEQ ID NO: 732)

5'-GAGCGACUGCCUGGUCUGCCGCAaa-3' (SEQ ID NO: 21)
3'-CUCUCGCUGACGGACCAGACGGCGUUU-5' (SEQ ID NO: 377)

EGFR-1005 Target: 5'-GAGAGCGACTGCTGGTCTGCCGCAA-3' (SEQ ID NO: 733)

5'-GCCUGGUCUGCCGCAAAUCCGAg-3' (SEQ ID NO: 22)

3'-GACGGACCAGACGGCGUUUAAGGCUCU-5' (SEQ ID NO: 378)
EGFR-1013 Target: 5'-CTGCCTGGTCTGCCGCAAATTCGAGA-3' (SEQ ID NO: 734)

5'-CAGAUACGGCUCGUGCGUCCGAgc-3' (SEQ ID NO: 23)
3'-CUGUCUAGUGCCGAGCACGCAGGCUCG-5' (SEQ ID NO: 379)
EGFR-1175 Target: 5'-GACAGATCACGGCTCGTGCGTCCGAGC-3' (SEQ ID NO: 735)

5'-GCAAAGUGUGUAACGGAAUAGGUat-3' (SEQ ID NO: 24)
3'-GGCGUUUCACACAUUGCCUUAUCCAUA-5' (SEQ ID NO: 380)
EGFR-1271 Target: 5'-CCGCAAAGTGTGTAACGGAATAGGTAT-3' (SEQ ID NO: 736)

5'-GAAUAGGUUAUUGGUGAAUUUAAAga-3' (SEQ ID NO: 25)
3'-GCCUUAUCCAUAACCACUUAUUUUUCU-5' (SEQ ID NO: 381)
EGFR-1286 Target: 5'-CGGAATAGGTATTGGTGAATTTAAAGA-3' (SEQ ID NO: 737)

5'-ACGAAUUAUAAACACUUCAAAAAct-3' (SEQ ID NO: 26)
3'-GAUGCUUAUAAUUUGUGAAGUUUUUGA-5' (SEQ ID NO: 382)
EGFR-1330 Target: 5'-CTACGAATATTAAACACTTCAAAAACT-3' (SEQ ID NO: 738)

5'-ACAGGAACUGGAUAUUCUGAAAAcc-3' (SEQ ID NO: 27)
3'-GGUGUCCUUGACCUAUAAGACUUUUGG-5' (SEQ ID NO: 383)
EGFR-1437 Target: 5'-CCACAGGAACTGGATATTCTGAAAACC-3' (SEQ ID NO: 739)

5'-CAGGGUUUUUGCUGAUUCAGGCutg-3' (SEQ ID NO: 28)
3'-GUGUCCCAAAAACGACUAAGUCCGAAC-5' (SEQ ID NO: 384)
EGFR-1475 Target: 5'-CACAGGGTTTTTGCTGATTCAGGCTTG-3' (SEQ ID NO: 740)

5'-CAGGAAACAAAAAUUUGUGCUAUgc-3' (SEQ ID NO: 29)
3'-AAGUCCUUUGUUUUUAAACACGAUACG-5' (SEQ ID NO: 385)
EGFR-1661 Target: 5'-TTCAGGAAACAAAAATTTGTGCTATGC-3' (SEQ ID NO: 741)

5'-GCUAUGCAAAUACAAUAAACUGGaa-3' (SEQ ID NO: 30)
3'-CACGAUACGUUUAUGUUAUUUGACCUU-5' (SEQ ID NO: 386)
EGFR-1679 Target: 5'-GTGCTATGCAAATACAATAAACTGGAA-3' (SEQ ID NO: 742)

5'-GGUCAGAAAACCAAAAUUAUAAGca-3' (SEQ ID NO: 31)
3'-GGCCCAGUCUUUUGGUUUUAUAUUCGU-5' (SEQ ID NO: 387)
EGFR-1723 Target: 5'-CCGGTCAGAAAACCAAAATTATAAGCA-3' (SEQ ID NO: 743)

5'-GCGUCUCUUGCCGGAAUGUCAGCcg-3' (SEQ ID NO: 32)
3'-GACGCAGAGAACGGCCUUAACAGUCGGC-5' (SEQ ID NO: 388)
EGFR-1838 Target: 5'-CTGCGTCTCTTGCCGGAATGTCAGCCG-3' (SEQ ID NO: 744)

5'-GCCCUCUUCUUGCUGCUGGUGGUgg-3' (SEQ ID NO: 33)
3'-CCCGGGAGGAGAACGACGACCACCACC-5' (SEQ ID NO: 389)
EGFR-2227 Target: 5'-GGGCCCTCCTCTTGCTGCTGGTGGTGG-3' (SEQ ID NO: 745)

5'-CCCUCUUCUUGCUGCUGGUGGUGgc-3' (SEQ ID NO: 34)
3'-CCGGGAGGAGAACGACGACCACCACCG-5' (SEQ ID NO: 390)
EGFR-2228 Target: 5'-GGCCCTCCTCTTGCTGCTGGTGGTGGC-3' (SEQ ID NO: 746)

5'-CCUCUUGCUGCUGGUGGUGGCCctg-3' (SEQ ID NO: 35)
3'-GAGGAGAACGACGACCACCACCGGGAC-5' (SEQ ID NO: 391)
EGFR-2232 Target: 5'-CTCCTCTTGCTGCTGGTGGTGGCCCTG-3' (SEQ ID NO: 747)

5'-CUCUUGCUGCUGGUGGUGGCCUgg-3' (SEQ ID NO: 36)
3'-AGGAGAACGACGACCACCACCGGGACC-5' (SEQ ID NO: 392)
EGFR-2233 Target: 5'-TCCTCTTGCTGCTGGTGGTGGCCCTGG-3' (SEQ ID NO: 748)

5'-GAAGCGCACGCUGCGGAGGCUGctg-3' (SEQ ID NO: 37)
3'-GCCUUCGCGUGCGACGCCUCCGACGAC-5' (SEQ ID NO: 393)
EGFR-2295 Target: 5'-CGGAAGCGCACGCTGCGGAGGCTGCTG-3' (SEQ ID NO: 749)

5'-GCGCACGCUGCGGAGGCUGCUGCag-3' (SEQ ID NO: 38)
3'-UUCGCGUGCGACGCCUCCGACGACGUC-5' (SEQ ID NO: 394)
EGFR-2298 Target: 5'-AAGCGCACGCTGCGGAGGCTGCTGCAG-3' (SEQ ID NO: 750)

5'-CUGAAUUCAAAAAGAUCAAAGUGct-3' (SEQ ID NO: 39)
3'-UUGACUUAAGUUUUUCUAGUUUCACGA-5' (SEQ ID NO: 395)
EGFR-2399 Target: 5'-AACTGAATTCAAAAAGATCAAAGTGCT-3' (SEQ ID NO: 751)

5'-AAGUGCUGGGCUCCGGUGCGUUCgg-3' (SEQ ID NO: 40)
3'-GUUUCACGACCCGAGGCCACGCAAGCC-5' (SEQ ID NO: 396)
EGFR-2417 Target: 5'-CAAAGTGCTGGGCTCCGGTGCGTTCGG-3' (SEQ ID NO: 752)

5'-GUGCUGGGCUCCGGUGCGUUCGGca-3' (SEQ ID NO: 41)
3'-UUCACGACCCGAGGCCACGCAAGCCGU-5' (SEQ ID NO: 397)
EGFR-2419 Target: 5'-AAGTGCTGGGCTCCGGTGCGTTCGGCA-3' (SEQ ID NO: 753)

5'-UGCUGGGCUCCGGUGCGUUCGGCac-3' (SEQ ID NO: 42)
3'-UCACGACCCGAGGCCACGCAAGCCGUG-5' (SEQ ID NO: 398)
EGFR-2420 Target: 5'-AGTGCTGGGCTCCGGTGCGTTCGGCAC-3' (SEQ ID NO: 754)

5'-GCUGGGCUCCGGUGCGUUCGGCAcg-3' (SEQ ID NO: 43)
3'-CACGACCCGAGGCCACGCAAGCCGUGC-5' (SEQ ID NO: 399)
EGFR-2421 Target: 5'-GTGCTGGGCTCCGGTGCGTTCGGCACG-3' (SEQ ID NO: 755)

5'-CUGGGCUCCGGUGCGUUCGGCACgg-3' (SEQ ID NO: 44)
3'-ACGACCCGAGGCCACGCAAGCCGUGCC-5' (SEQ ID NO: 400)
EGFR-2422 Target: 5'-TGCTGGGCTCCGGTGCGTTCGGCACGG-3' (SEQ ID NO: 756)

5'-UGUGCCGCCUGCUGGGCAUCUGCct-3' (SEQ ID NO: 45)
3'-GCACACGGCGGACGACCCGUAGACGGA-5' (SEQ ID NO: 401)
EGFR-2591 Target: 5'-CGTGTGCCGCTGCTGGGCATCTGCCT-3' (SEQ ID NO: 757)

5'-GUGCCGCCUGCUGGGCAUCUGCCtc-3' (SEQ ID NO: 46)
3'-CACACGGCGGACGACCCGUAGACGGAG-5' (SEQ ID NO: 402)
EGFR-2592 Target: 5'-GTGTGCCGCCTGCTGGGCATCTGCCTC-3' (SEQ ID NO: 758)

5'-GCCGCCUGCUGGGCAUCUGCCUCac-3' (SEQ ID NO: 47)
3'-CACGGCGGACGACCCGUAGACGGAGUG-5' (SEQ ID NO: 403)
EGFR-2594 Target: 5'-GTGCCGCCTGCTGGGCATCTGCCTCAC-3' (SEQ ID NO: 759)

5'-CCGUGCAGCUCAUCACGCAGCUCat-3' (SEQ ID NO: 48)
3'-GUGGCACGUCGAGUAGUGCGUCGAGUA-5' (SEQ ID NO: 404)
EGFR-2624 Target: 5'-CACCGTGCAGCTCATCACGCAGCTCAT-3' (SEQ ID NO: 760)

5'-UGCAGCUCAUCACGCAGCUCAUGcc-3' (SEQ ID NO: 49)
3'-GCACGUCGAGUAGUGCGUCGAGUACGG-5' (SEQ ID NO: 405)
EGFR-2627 Target: 5'-CGTGCAGCTCATCACGCAGCTCATGCC-3' (SEQ ID NO: 761)

5'-GCUCAUCACGCAGCUCAUGCCCUtc-3' (SEQ ID NO: 50)
3'-GUCGAGUAGUGCGUCGAGUACGGGAAG-5' (SEQ ID NO: 406)
EGFR-2631 Target: 5'-CAGCTCATCACGCAGCTCATGCCCTTC-3' (SEQ ID NO: 762)

5'-CUCAUCACGCAGCUCAUGCCCUUcg-3' (SEQ ID NO: 51)
3'-UCGAGUAGUGCGUCGAGUACGGGAAGC-5' (SEQ ID NO: 407)
EGFR-2632 Target: 5'-AGCTCATCACGCAGCTCATGCCCTTCG-3' (SEQ ID NO: 763)

5'-GCUCAUGCCCUUCGGCUGCCUCctg-3' (SEQ ID NO: 52)
3'-GUCGAGUACGGGAAGCCGACGGAGGAC-5' (SEQ ID NO: 408)
EGFR-2643 Target: 5'-CAGCTCATGCCCTTCGGCTGCCTCCTG-3' (SEQ ID NO: 764)

5'-CUCAUGCCCUUCGGCUGCCUCCUgg-3' (SEQ ID NO: 53)
3'-UCGAGUACGGGAAGCCGACGGAGGACC-5' (SEQ ID NO: 409)
EGFR-2644 Target: 5'-AGCTCATGCCCTTCGGCTGCCTCCTGG-3' (SEQ ID NO: 765)

5'-GGAGGACCGUCGCUUGGUGCACCgc-3' (SEQ ID NO: 54)
3'-AACCUCCUGGCAGCGAACCACGUGGCG-5' (SEQ ID NO: 410)
EGFR-2754 Target: 5'-TTGGAGGACCGTCGCTTGGTGCACCGC-3' (SEQ ID NO: 766)

5'-AGGACCGUCGCUUGGUGCACCgcga-3' (SEQ ID NO: 55)
3'-CCUCCUGGCAGCGAACCACGUGGCGCU-5' (SEQ ID NO: 411)
EGFR-2756 Target: 5'-GGAGGACCGTCGCTTGGTGCACCGCGA-3' (SEQ ID NO: 767)

5'-GGACCGUCGCUUGGUGCACCgcGac-3' (SEQ ID NO: 56)
3'-CUCCUGGCAGCGAACCACGUGGCGCUG-5' (SEQ ID NO: 412)
EGFR-2757 Target: 5'-GAGGACCGTCGCTTGGTGCACCGCGAC-3' (SEQ ID NO: 768)

5'-GACCGUCGCUUGGUGCACCgcGacc-3' (SEQ ID NO: 57)
3'-UCCUGGCAGCGAACCACGUGGCGCUGG-5' (SEQ ID NO: 413)

EGFR-2758 Target: 5'-AGGACCGTCGCTTGGTGCACCGCGACC-3' (SEQ ID NO: 769)

5'-CCGUCGCUUGGUGCACCGCGACctg-3' (SEQ ID NO: 58)
3'-CUGGCAGCGAACCACGUGGCGCUGGAC-5' (SEQ ID NO: 414)

EGFR-2760 Target: 5'-GACCGTCGCTTGGTGCACCGCGACCTG-3' (SEQ ID NO: 770)

5'-GUCGCUUGGUGCACCGCGACCUGgc-3' (SEQ ID NO: 59)
3'-GGCAGCGAACCACGUGGCGCUGGACCG-5' (SEQ ID NO: 415)

EGFR-2762 Target: 5'-CCGTCGCTTGGTGCACCGCGACCTGGC-3' (SEQ ID NO: 771)

5'-CGCUUGGUGCACCGCGACCUGGCag-3' (SEQ ID NO: 60)
3'-CAGCGAACCACGUGGCGCUGGACCGUC-5' (SEQ ID NO: 416)

EGFR-2764 Target: 5'-GTCGCTTGGTGCACCGCGACCTGGCAG-3' (SEQ ID NO: 772)

5'-GCUUGGUGCACCGCGACCUGGCAGc-3' (SEQ ID NO: 61)
3'-AGCGAACCACGUGGCGCUGGACCGUCG-5' (SEQ ID NO: 417)

EGFR-2765 Target: 5'-TCGCTTGGTGCACCGCGACCTGGCAGC-3' (SEQ ID NO: 773)

5'-UUGGUGCACCGCGACCUGGCAGCca-3' (SEQ ID NO: 62)
3'-CGAACCACGUGGCGCUGGACCGUCGGU-5' (SEQ ID NO: 418)

EGFR-2767 Target: 5'-GCTTGGTGCACCGCGACCTGGCAGCCA-3' (SEQ ID NO: 774)

5'-CAUUGGAAUCAUUUUUACACAGAat-3' (SEQ ID NO: 63)
3'-CCGUAACCUUAGUUAUUUUUGUGUCUUA-5' (SEQ ID NO: 419)

EGFR-2915 Target: 5'-GGCATTGGAATCAATTTTACACAGAAT-3' (SEQ ID NO: 775)

5'-AAGUGCUGGAUGAUAGACGCAGAta-3' (SEQ ID NO: 64)
3'-AGUUCACGACCUACUAUCUGCGUCUAU-5' (SEQ ID NO: 420)

EGFR-3115 Target: 5'-TCAAGTGCTGGATGATAGACGCAGATA-3' (SEQ ID NO: 776)

5'-GUGCUGGAUGAUAGACGCAGAUAgT-3' (SEQ ID NO: 65)
3'-UUCACGACCUACUAUCUGCGUCUAUCA-5' (SEQ ID NO: 421)

EGFR-3117 Target: 5'-AAGTGCTGGATGATAGACGCAGATAGT-3' (SEQ ID NO: 777)

5'-UGCUGGAUGAUAGACGCAGAUAGtc-3' (SEQ ID NO: 66)
3'-UCACGACCUACUAUCUGCGUCUAUCAG-5' (SEQ ID NO: 422)

EGFR-3118 Target: 5'-AGTGCTGGATGATAGACGCAGATAGTC-3' (SEQ ID NO: 778)

5'-CUGGAUGAUAGACGCAGAUAGUCgc-3' (SEQ ID NO: 67)
3'-ACGACCUACUAUCUGCGUCUAUCAGCG-5' (SEQ ID NO: 423)

EGFR-3120 Target: 5'-TGCTGGATGATAGACGCAGATAGTCGC-3' (SEQ ID NO: 779)

5'-CCUGAGCUCUCUGAGUGCAACCAgc-3' (SEQ ID NO: 68)
3'-GAGGACUCGAGAGACUCACGUUGGUCG-5' (SEQ ID NO: 424)

EGFR-3372 Target: 5'-CTCCTGAGCTCTCTGAGTGCAACCAGC-3' (SEQ ID NO: 780)

5'-GAGCUCUCUGAGUGCAACCAGCAac-3' (SEQ ID NO: 69)

3'-GACUCGAGAGACUCACGUUGGUCGUUG-5' (SEQ ID NO: 425)
EGFR-3375 Target: 5'-CTGAGCTCTCTGAGTGCAACCAGCAAC-3' (SEQ ID NO: 781)

5'-GCUGUCCCAUCAAGGAAGACAGCtt-3' (SEQ ID NO: 70)
3'-UUCGACAGGGUAGUCCUUCUGUCGAA-5' (SEQ ID NO: 426)
EGFR-3440 Target: 5'-AAGCTGTCCCATCAAGGAAGACAGCTT-3' (SEQ ID NO: 782)

5'-CUGUCCCAUCAAGGAAGACAGCUtc-3' (SEQ ID NO: 71)
3'-UCGACAGGGUAGUCCUUCUGUCGAAG-5' (SEQ ID NO: 427)
EGFR-3441 Target: 5'-AGCTGTCCCATCAAGGAAGACAGCTTC-3' (SEQ ID NO: 783)

5'-GACAGCUUCUUGCAGCGAUACAGct-3' (SEQ ID NO: 72)
3'-UUCUGUCGAAGAACGUCGCUAUGUCGA-5' (SEQ ID NO: 428)
EGFR-3457 Target: 5'-AAGACAGCTTCTTGCAGCGATACAGCT-3' (SEQ ID NO: 784)

5'-ACAGCUUCUUGCAGCGAUACAGCtc-3' (SEQ ID NO: 73)
3'-UCUGUCGAAGAACGUCGCUAUGUCGAG-5' (SEQ ID NO: 429)
EGFR-3458 Target: 5'-AGACAGCTTCTTGCAGCGATACAGCTC-3' (SEQ ID NO: 785)

5'-CAGCUUCUUGCAGCGAUACAGCUca-3' (SEQ ID NO: 74)
3'-CUGUCGAAGAACGUCGCUAUGUCGAGU-5' (SEQ ID NO: 430)
EGFR-3459 Target: 5'-GACAGCTTCTTGCAGCGATACAGCTCA-3' (SEQ ID NO: 786)

5'-AGCUUCUUGCAGCGAUACAGCUCag-3' (SEQ ID NO: 75)
3'-UGUCGAAGAACGUCGCUAUGUCGAGUC-5' (SEQ ID NO: 431)
EGFR-3460 Target: 5'-ACAGCTTCTTGCAGCGATACAGCTCAG-3' (SEQ ID NO: 787)

5'-GCUUCUUGCAGCGAUACAGCUCaga-3' (SEQ ID NO: 76)
3'-GUCGAAGAACGUCGCUAUGUCGAGUCU-5' (SEQ ID NO: 432)
EGFR-3461 Target: 5'-CAGCTTCTTGCAGCGATACAGCTCAGA-3' (SEQ ID NO: 788)

5'-UUCUUGCAGCGAUACAGCUCAGacc-3' (SEQ ID NO: 77)
3'-CGAAGAACGUCGCUAUGUCGAGUCUGG-5' (SEQ ID NO: 433)
EGFR-3463 Target: 5'-GCTTCTTGCAGCGATACAGCTCAGACC-3' (SEQ ID NO: 789)

5'-ACAAAGCAGUGAAUUUAUUGGAGca-3' (SEQ ID NO: 78)
3'-GGUGUUUCGUCACUUAUAUAACCUCGU-5' (SEQ ID NO: 434)
EGFR-3876 Target: 5'-CCACAAAGCAGTGAATTTATTGGAGCA-3' (SEQ ID NO: 790)

5'-AUUUUUGAAAAAAAAAAAAAGUAta-3' (SEQ ID NO: 79)
3'-CAUAUAACUUUUUUUUUUUUUCAUAU-5' (SEQ ID NO: 435)
EGFR-4178 Target: 5'-GTATATTTGAAAAAAAAAAAAAGTATA-3' (SEQ ID NO: 791)

5'-UGAGGAUUUUUAUUGAUUGGGGAtc-3' (SEQ ID NO: 80)
3'-ACACUCCUAAAAUAACUAACCCCUAG-5' (SEQ ID NO: 436)
EGFR-4205 Target: 5'-TGTGAGGATTTTTATTGATTGGGGATC-3' (SEQ ID NO: 792)

5'-CUAUUGAUUUUUACUCAAUGGGct-3' (SEQ ID NO: 81)
3'-GCGAUAACUAAAAUGAAGUUACCCGA-5' (SEQ ID NO: 437)
EGFR-4249 Target: 5'-CGCTATTGATTTTTACTTCAATGGGCT-3' (SEQ ID NO: 793)

5'-GGAAGAAGCUUGCUGGUAGCACUtg-3' (SEQ ID NO: 82)
3'-UUCCUUCUUCGAACGACCAUCGUGAAC-5' (SEQ ID NO: 438)
EGFR-4284 Target: 5'-AAGGAAGAAGCTTGCTGGTAGCACTTG-3' (SEQ ID NO: 794)

5'-GAAGAAGCUUGCUGGUAGCACUUGC-3' (SEQ ID NO: 83)
3'-UCCUUCUUCGAACGACCAUCGUGAACG-5' (SEQ ID NO: 439)
EGFR-4285 Target: 5'-AGGAAGAAGCTTGCTGGTAGCACTTGC-3' (SEQ ID NO: 795)

5'-AAGAAGCUUGCUGGUAGCACUUGct-3' (SEQ ID NO: 84)
3'-CCUUCUUCGAACGACCAUCGUGAACGA-5' (SEQ ID NO: 440)
EGFR-4286 Target: 5'-GGAAGAAGCTTGCTGGTAGCACTTGCT-3' (SEQ ID NO: 796)

5'-AGAAGCUUGCUGGUAGCACUUGCta-3' (SEQ ID NO: 85)
3'-CUUCUUCGAACGACCAUCGUGAACGAU-5' (SEQ ID NO: 441)
EGFR-4287 Target: 5'-GAAGAAGCTTGCTGGTAGCACTTGCTA-3' (SEQ ID NO: 797)

5'-GAAGCUUGCUGGUAGCACUUGCUac-3' (SEQ ID NO: 86)
3'-UUCUUCGAACGACCAUCGUGAACGAUG-5' (SEQ ID NO: 442)
EGFR-4288 Target: 5'-AAGAAGCTTGCTGGTAGCACTTGCTAC-3' (SEQ ID NO: 798)

5'-AGCUUGCUGGUAGCACUUGCUCACcc-3' (SEQ ID NO: 87)
3'-CUUCGAACGACCAUCGUGAACGAUGGG-5' (SEQ ID NO: 443)
EGFR-4290 Target: 5'-GAAGCTTGCTGGTAGCACTTGCTACCC-3' (SEQ ID NO: 799)

5'-GCUUGCUGGUAGCACUUGCUCACCct-3' (SEQ ID NO: 88)
3'-UUCGAACGACCAUCGUGAACGAUGGGA-5' (SEQ ID NO: 444)
EGFR-4291 Target: 5'-AAGCTTGCTGGTAGCACTTGCTACCCT-3' (SEQ ID NO: 800)

5'-CUUGCUGGUAGCACUUGCUCACCctg-3' (SEQ ID NO: 89)
3'-UCGAACGACCAUCGUGAACGAUGGGAC-5' (SEQ ID NO: 445)
EGFR-4292 Target: 5'-AGCTTGCTGGTAGCACTTGCTACCCTG-3' (SEQ ID NO: 801)

5'-UUGCUGGUAGCACUUGCUCACCCUga-3' (SEQ ID NO: 90)
3'-CGAACGACCAUCGUGAACGAUGGGACU-5' (SEQ ID NO: 446)
EGFR-4293 Target: 5'-GCTTGCTGGTAGCACTTGCTACCCTGA-3' (SEQ ID NO: 802)

5'-UGCUGGUAGCACUUGCUCACCCUGag-3' (SEQ ID NO: 91)
3'-GAACGACCAUCGUGAACGAUGGGACUC-5' (SEQ ID NO: 447)
EGFR-4294 Target: 5'-CTTGCTGGTAGCACTTGCTACCCTGAG-3' (SEQ ID NO: 803)

5'-GCUGGUAGCACUUGCUCACCCUGAgt-3' (SEQ ID NO: 92)
3'-AACGACCAUCGUGAACGAUGGGACUCA-5' (SEQ ID NO: 448)
EGFR-4295 Target: 5'-TTGCTGGTAGCACTTGCTACCCTGAGT-3' (SEQ ID NO: 804)

5'-AUGCUUGAUUCCAGUGGUUCUGCtt-3' (SEQ ID NO: 93)
3'-CCUACGAACUAAGGUCACCAAGACGAA-5' (SEQ ID NO: 449)
EGFR-4372 Target: 5'-GGATGCTTGATTCCAGTGGTTCTGCTT-3' (SEQ ID NO: 805)

5'-UGCUUGAUUCCAGUGGUUCUGCUtc-3' (SEQ ID NO: 94)
3'-CUACGAACUAAGGUCACCAAGACGAAG-5' (SEQ ID NO: 450)
EGFR-4373 Target: 5'-GATGCTTGATTCCAGTGGTTCTGCTTC-3' (SEQ ID NO: 806)

5'-CAGGCCGGAUCGGUACUGUAUCAag-3' (SEQ ID NO: 95)
3'-UCGUCCGGCCUAGCCAUGACAUAUUC-5' (SEQ ID NO: 451)
EGFR-4450 Target: 5'-AGCAGGCCGGATCGGTACTGTATCAAG-3' (SEQ ID NO: 807)

5'-CGGAUCGGUACUGUAUCAAGUCAtg-3' (SEQ ID NO: 96)
3'-CGGCCUAGCCAUGACAUAUUCAGUAC-5' (SEQ ID NO: 452)
EGFR-4455 Target: 5'-GCCGGATCGGTACTGTATCAAGTCATG-3' (SEQ ID NO: 808)

5'-CUUAGACUUACUUUUGUAAAAAUgt-3' (SEQ ID NO: 97)
3'-AGGAUCUGAAUGAAAACAUUUUUACA-5' (SEQ ID NO: 453)
EGFR-4550 Target: 5'-TCCTTAGACTTACTTTTGTAAAAATGT-3' (SEQ ID NO: 809)

5'-GUCUUGCUGUCAUGAAAUCAGCAag-3' (SEQ ID NO: 98)
3'-GACAGAACGACAGUACUUUAGUCGUUC-5' (SEQ ID NO: 454)
EGFR-4684 Target: 5'-CTGTCTTGCTGTTCATGAAATCAGCAAG-3' (SEQ ID NO: 810)

5'-UAAGGAUAGCACCGCUUUUGUUCtc-3' (SEQ ID NO: 99)
3'-GGAUCCUAUCGUGGCGAAAACAAGAG-5' (SEQ ID NO: 455)
EGFR-4804 Target: 5'-CCTAAGGATAGCACCGCTTTTGTTC-3' (SEQ ID NO: 811)

5'-AGGAUAGCACCGCUUUUGUUCUCgc-3' (SEQ ID NO: 100)
3'-AUUCCUAUCGUGGCGAAAACAAGAGCG-5' (SEQ ID NO: 456)
EGFR-4806 Target: 5'-TAAGGATAGCACCGCTTTTGTTCGCG-3' (SEQ ID NO: 812)

5'-GGAUAGCACCGCUUUUGUUCUCGca-3' (SEQ ID NO: 101)
3'-UUCCUAUCGUGGCGAAAACAAGAGCGU-5' (SEQ ID NO: 457)
EGFR-4807 Target: 5'-AAGGATAGCACCGCTTTTGTTCGCA-3' (SEQ ID NO: 813)

5'-GAUAGCACCGCUUUUGUUCUCGCaa-3' (SEQ ID NO: 102)
3'-UCCUAUCGUGGCGAAAACAAGAGCGUU-5' (SEQ ID NO: 458)
EGFR-4808 Target: 5'-AGGATAGCACCGCTTTTGTTCGCAA-3' (SEQ ID NO: 814)

5'-AUAGCACCGCUUUUGUUCUCGCAaa-3' (SEQ ID NO: 103)
3'-CCUAUCGUGGCGAAAACAAGAGCGUUU-5' (SEQ ID NO: 459)
EGFR-4809 Target: 5'-GGATAGCACCGCTTTTGTTCGCAAA-3' (SEQ ID NO: 815)

5'-UAGCACCGCUUUUGUUCUCGCAaaa-3' (SEQ ID NO: 104)
3'-CUAUCGUGGCGAAAACAAGAGCGUUUU-5' (SEQ ID NO: 460)

EGFR-4810 Target: 5'-GATAGCACCGCTTTTGTCTCGCAAAA-3' (SEQ ID NO: 816)

5'-AGCACCGCUUUUGUUCUCGCAAAAa-3' (SEQ ID NO: 105)

3'-UAUCGUGGCGAAAAACAAGAGCGUUUUU-5' (SEQ ID NO: 461)

EGFR-4811 Target: 5'-ATAGCACCGCTTTTGTCTCGCAAAA-3' (SEQ ID NO: 817)

5'-GCACCGCUUUUGUUCUCGCAAAAac-3' (SEQ ID NO: 106)

3'-AUCGUGGCGAAAAACAAGAGCGUUUUUG-5' (SEQ ID NO: 462)

EGFR-4812 Target: 5'-TAGCACCGCTTTTGTCTCGCAAAAAC-3' (SEQ ID NO: 818)

5'-CACCGCUUUUGUUCUCGCAAAAacg-3' (SEQ ID NO: 107)

3'-UCGUGGCGAAAAACAAGAGCGUUUUUGC-5' (SEQ ID NO: 463)

EGFR-4813 Target: 5'-AGCACCGCTTTTGTCTCGCAAAAACG-3' (SEQ ID NO: 819)

5'-CGCUUUUGUUCUCGCAAAAACGUat-3' (SEQ ID NO: 108)

3'-UGGCGAAAAACAAGAGCGUUUUUGCAUA-5' (SEQ ID NO: 464)

EGFR-4816 Target: 5'-ACCGCTTTTGTCTCGCAAAAACGTAT-3' (SEQ ID NO: 820)

5'-GCUUUUGUUCUCGCAAAAACGUatc-3' (SEQ ID NO: 109)

3'-GGCGAAAAACAAGAGCGUUUUUGCAUAG-5' (SEQ ID NO: 465)

EGFR-4817 Target: 5'-CCGCTTTTGTCTCGCAAAAACGTATC-3' (SEQ ID NO: 821)

5'-CUUUUGUUCUCGCAAAAACGUAUct-3' (SEQ ID NO: 110)

3'-GCGAAAAACAAGAGCGUUUUUGCAUAGA-5' (SEQ ID NO: 466)

EGFR-4818 Target: 5'-CGCTTTTGTCTCGCAAAAACGTATCT-3' (SEQ ID NO: 822)

5'-UUUUGUUCUCGCAAAAACGUAUctc-3' (SEQ ID NO: 111)

3'-CGAAAAACAAGAGCGUUUUUGCAUAGAG-5' (SEQ ID NO: 467)

EGFR-4819 Target: 5'-GCTTTTGTCTCGCAAAAACGTATCTC-3' (SEQ ID NO: 823)

5'-UUCUCGCAAAAACGUAUCCUAat-3' (SEQ ID NO: 112)

3'-ACAAGAGCGUUUUUGCAUAGAGGAUUA-5' (SEQ ID NO: 468)

EGFR-4824 Target: 5'-TGTTCTCGCAAAAACGTATCTCCTAAT-3' (SEQ ID NO: 824)

5'-AAAUUAGUUUGUGUUACUUAUGGaa-3' (SEQ ID NO: 113)

3'-GUUUUAAUCAAACACAAUGAAUACCUU-5' (SEQ ID NO: 469)

EGFR-4953 Target: 5'-CAAAATTAGTTTGTGTTACTTATGGAA-3' (SEQ ID NO: 825)

5'-UUAUGGAAGAUAGUUUUCUCCUUt-3' (SEQ ID NO: 114)

3'-UGAAUACCUUCUAUCAAAGAGGAAAA-5' (SEQ ID NO: 470)

EGFR-4970 Target: 5'-ACTTATGGAAGATAGTTTTCTCCTTTT-3' (SEQ ID NO: 826)

5'-UCAAAAGCUUUUACUCAAGAGta-3' (SEQ ID NO: 115)

3'-GAAGUUUCGAAAAAUGAGUUUCUCAU-5' (SEQ ID NO: 471)

EGFR-5003 Target: 5'-CTTCAAAGCTTTTACTCAAAGAGTA-3' (SEQ ID NO: 827)

5'-ACUAGGGUUUGAAAUUGAUAAUGct-3' (SEQ ID NO: 116)

3'-UUUGAUCCCAAACUUUAACUAUUACGA-5' (SEQ ID NO: 472)
EGFR-5206 Target: 5'-AAACTAGGGTTTGAAATTGATAATGCT-3' (SEQ ID NO: 828)

5'-UAAAAUAAUUUCUCUACAAUUGGaa-3' (SEQ ID NO: 117)
3'-GGAUUUUUAAUAAAGAGAUGUUAACCUU-5' (SEQ ID NO: 473)
EGFR-5275 Target: 5'-CCTAAAATAATTTCTCTACAATTGGAA-3' (SEQ ID NO: 829)

5'-CAGCAGUCCUUUGUAAACAGUGUtt-3' (SEQ ID NO: 118)
3'-UUGUCGUCAGGAAACAUUUGUCACAAA-5' (SEQ ID NO: 474)
EGFR-5374 Target: 5'-AACAGCAGTCCTTTGTAAACAGTGTTT-3' (SEQ ID NO: 830)

5'-CAAUUUAUCAAGGAAGAAAUGGUtc-3' (SEQ ID NO: 119)
3'-AGGUUAAAAGUUCUUCUUAACCAAG-5' (SEQ ID NO: 475)
EGFR-5429 Target: 5'-TCCAATTTATCAAGGAAGAAATGGTTC-3' (SEQ ID NO: 831)

5'-UACAAAAUGUCCUUUUUGCUUUUaa-3' (SEQ ID NO: 120)
3'-GUAUGUUUUACAAGGAAAACGAAAAUU-5' (SEQ ID NO: 476)
EGFR-5497 Target: 5'-CATACAAAATGTTCTTTTGCTTTTAA-3' (SEQ ID NO: 832)

5'-GUUCCUUUUGCUUUUAAAGUAAUtt-3' (SEQ ID NO: 121)
3'-UACAAGGAAAACGAAAUUUCAUUAAA-5' (SEQ ID NO: 477)
EGFR-5505 Target: 5'-ATGTTCTTTTGCTTTTAAAGTAATTT-3' (SEQ ID NO: 833)

5'-UUCCUUUUGCUUUUAAAGUAAUtt-3' (SEQ ID NO: 122)
3'-ACAAGGAAAACGAAAUUUCAUUAAA-5' (SEQ ID NO: 478)
EGFR-5506 Target: 5'-TGTTCTTTTGCTTTTAAAGTAATTTT-3' (SEQ ID NO: 834)

5'-UUGCUUUUAAAGUAAUUUUUGACTc-3' (SEQ ID NO: 123)
3'-AAAACGAAAUUUCAUUAAAACUGAG-5' (SEQ ID NO: 479)
EGFR-5512 Target: 5'-TTTTGCTTTTAAAGTAATTTTGAATC-3' (SEQ ID NO: 835)

5'-GUUAAGAAAGUAAUUUGAUUUUUGtc-3' (SEQ ID NO: 124)
3'-AACAAUUCUUUCAUAAACUAAAAACAG-5' (SEQ ID NO: 480)
EGFR-5565 Target: 5'-TTGTTAAGAAAGTATTTGATTTTGTGTC-3' (SEQ ID NO: 836)

5'-UUGGAAAUUACCUAUGUGCAGAGga-3' (SEQ ID NO: 125)
3'-UAAACCUUUAAUGGAUACACGUCUCCU-5' (SEQ ID NO: 481)
EGFR-463 Target: 5'-ATTTGGAAATTACCTATGTGCAGAGGA-3' (SEQ ID NO: 837)

5'-UGGAAAUUACCUAUGUGCAGAGGaa-3' (SEQ ID NO: 126)
3'-AAACCUUUAAUGGAUACACGUCUCCU-5' (SEQ ID NO: 482)
EGFR-464 Target: 5'-TTTGGAAATTACCTATGTGCAGAGGAA-3' (SEQ ID NO: 838)

5'-CUUCCUUCUUAAGACCAUCCAgg-3' (SEQ ID NO: 127)
3'-UAGAAAGGAAGAAUUUCUGGUAGGUCC-5' (SEQ ID NO: 483)
EGFR-496 Target: 5'-ATCTTTCCTTCTTAAAGACCATCCAGG-3' (SEQ ID NO: 839)

5'-UUUCCUUCUAAAAGACCAUCCAGga-3' (SEQ ID NO: 128)
3'-AGAAAGGAAGAAUUUCUGGUAGGUCCU-5' (SEQ ID NO: 484)
EGFR-497 Target: 5'-TCTTCCTTCTTAAAGACCATCCAGGA-3' (SEQ ID NO: 840)

5'-UUCUUCUAAAAGACCAUCCAGGag-3' (SEQ ID NO: 129)
3'-GAAAGGAAGAAUUUCUGGUAGGUCCUC-5' (SEQ ID NO: 485)
EGFR-498 Target: 5'-CTTTCCTTCTTAAAGACCATCCAGGAG-3' (SEQ ID NO: 841)

5'-UCCUUCUAAAAGACCAUCCAGGAgg-3' (SEQ ID NO: 130)
3'-AAAGGAAGAAUUUCUGGUAGGUCCUCC-5' (SEQ ID NO: 486)
EGFR-499 Target: 5'-TTTCCTTCTTAAAGACCATCCAGGAGG-3' (SEQ ID NO: 842)

5'-CCUUCUAAAAGACCAUCCAGGAGgt-3' (SEQ ID NO: 131)
3'-AAGGAAGAAUUUCUGGUAGGUCCUCCA-5' (SEQ ID NO: 487)
EGFR-500 Target: 5'-TTCCTTCTTAAAGACCATCCAGGAGGT-3' (SEQ ID NO: 843)

5'-CUUCUAAAAGACCAUCCAGGAGGtg-3' (SEQ ID NO: 132)
3'-AGGAAGAAUUUCUGGUAGGUCCUCCAC-5' (SEQ ID NO: 488)
EGFR-501 Target: 5'-TCCTTCTTAAAGACCATCCAGGAGGTG-3' (SEQ ID NO: 844)

5'-UUCUAAAAGACCAUCCAGGAGGUgg-3' (SEQ ID NO: 133)
3'-GGAAGAAUUUCUGGUAGGUCCUCCACC-5' (SEQ ID NO: 489)
EGFR-502 Target: 5'-CCTTCTTAAAGACCATCCAGGAGGTGG-3' (SEQ ID NO: 845)

5'-UCUAAAAGACCAUCCAGGAGGUGgc-3' (SEQ ID NO: 134)
3'-GAAGAUUUCUGGUAGGUCCUCCACCG-5' (SEQ ID NO: 490)
EGFR-503 Target: 5'-CTTCTTAAAGACCATCCAGGAGGTGGC-3' (SEQ ID NO: 846)

5'-CUAAAAGACCAUCCAGGAGGUGGct-3' (SEQ ID NO: 135)
3'-AAGAUUUCUGGUAGGUCCUCCACCGA-5' (SEQ ID NO: 491)
EGFR-504 Target: 5'-TTCTTAAAGACCATCCAGGAGGTGGCT-3' (SEQ ID NO: 847)

5'-UAAAAGACCAUCCAGGAGGUGGctg-3' (SEQ ID NO: 136)
3'-AGAAUUUCUGGUAGGUCCUCCACCGAC-5' (SEQ ID NO: 492)
EGFR-505 Target: 5'-TCTTAAAGACCATCCAGGAGGTGGCTG-3' (SEQ ID NO: 848)

5'-UAAAGACCAUCCAGGAGGUGGCUgg-3' (SEQ ID NO: 137)
3'-GAAUUUCUGGUAGGUCCUCCACCGACC-5' (SEQ ID NO: 493)
EGFR-506 Target: 5'-CTTAAAGACCATCCAGGAGGTGGCTGG-3' (SEQ ID NO: 849)

5'-AAAGACCAUCCAGGAGGUGGCUGgt-3' (SEQ ID NO: 138)
3'-AAUUUCUGGUAGGUCCUCCACCGACCA-5' (SEQ ID NO: 494)
EGFR-507 Target: 5'-TTAAAGACCATCCAGGAGGTGGCTGGT-3' (SEQ ID NO: 850)

5'-AAGACCAUCCAGGAGGUGGCUGGtt-3' (SEQ ID NO: 139)
3'-AUUUUCUGGUAGGUCCUCCACCGACCAA-5' (SEQ ID NO: 495)
EGFR-508 Target: 5'-TAAAGACCATCCAGGAGGTGGCTGGTT-3' (SEQ ID NO: 851)

5'-AGACCAUCCAGGAGGUGGCUUGGa-3' (SEQ ID NO: 140)
3'-UUUCUGGUAGGUUCCACCGACCAAU-5' (SEQ ID NO: 496)
EGFR-509 Target: 5'-AAAGACCATCCAGGAGGTGGCTGGTTA-3' (SEQ ID NO: 852)

5'-UGUGAUCCAAGCUGUCCCAAUGGga-3' (SEQ ID NO: 141)
3'-UCACACUAGGUUCGACAGGGUUACCCU-5' (SEQ ID NO: 497)
EGFR-838 Target: 5'-AGTGTGATCCAAGCTGTCCCAATGGGA-3' (SEQ ID NO: 853)

5'-GUGAUCCAAGCUGUCCCAAUGGGag-3' (SEQ ID NO: 142)
3'-CACACUAGGUUCGACAGGGUUACCCUC-5' (SEQ ID NO: 498)
EGFR-839 Target: 5'-GTGTGATCCAAGCTGTCCCAATGGGAG-3' (SEQ ID NO: 854)

5'-UGAUCCAAGCUGUCCCAAUGGGAgc-3' (SEQ ID NO: 143)
3'-ACACUAGGUUCGACAGGGUUACCCUCG-5' (SEQ ID NO: 499)
EGFR-840 Target: 5'-TGTGATCCAAGCTGTCCCAATGGGAGC-3' (SEQ ID NO: 855)

5'-GAUCCAAGCUGUCCCAAUGGGAGct-3' (SEQ ID NO: 144)
3'-CACUAGGUUCGACAGGGUUACCCUCGA-5' (SEQ ID NO: 500)
EGFR-841 Target: 5'-GTGATCCAAGCTGTCCCAATGGGAGCT-3' (SEQ ID NO: 856)

5'-AUCCAAGCUGUCCCAAUGGGAGCtg-3' (SEQ ID NO: 145)
3'-ACUAGGUUCGACAGGGUUACCCUCGAC-5' (SEQ ID NO: 501)
EGFR-842 Target: 5'-TGATCCAAGCTGTCCCAATGGGAGCTG-3' (SEQ ID NO: 857)

5'-AGGAGAGGAGAACUGCCAGAAActg-3' (SEQ ID NO: 146)
3'-CGUCCUCUCCUCUUGACGGUCUUUGAC-5' (SEQ ID NO: 502)
EGFR-876 Target: 5'-GCAGGAGAGGAGAACTGCCAGAAACTG-3' (SEQ ID NO: 858)

5'-GGAGAGGAGAACUGCCAGAAACUga-3' (SEQ ID NO: 147)
3'-GUCCUCUCCUCUUGACGGUCUUUGACU-5' (SEQ ID NO: 503)
EGFR-877 Target: 5'-CAGGAGAGGAGAACTGCCAGAAACTGA-3' (SEQ ID NO: 859)

5'-GAGAGGAGAACUGCCAGAAACUGac-3' (SEQ ID NO: 148)
3'-UCCUCUCCUCUUGACGGUCUUUGACUG-5' (SEQ ID NO: 504)
EGFR-878 Target: 5'-AGGAGAGGAGAACTGCCAGAAACTGAC-3' (SEQ ID NO: 860)

5'-AGAGGAGAACUGCCAGAAACUGAcc-3' (SEQ ID NO: 149)
3'-CCUCUCCUCUUGACGGUCUUUGACUGG-5' (SEQ ID NO: 505)
EGFR-879 Target: 5'-GGAGAGGAGAACTGCCAGAAACTGACC-3' (SEQ ID NO: 861)

5'-UGACCAAAAUCAUCUGUGCCCAGca-3' (SEQ ID NO: 150)
3'-UGACUGGUUUUAGUAGACACGGGUCGU-5' (SEQ ID NO: 506)
EGFR-899 Target: 5'-ACTGACCAAAATCATCTGTGCCAGCA-3' (SEQ ID NO: 862)

5'-GACCAAAAUCAUCUGUGCCCAGCag-3' (SEQ ID NO: 151)
3'-GACUGGUUUUAGUAGACACGGGUCGUC-5' (SEQ ID NO: 507)

EGFR-900 Target: 5'-CTGACCAAAATCATCTGTGCCCAGCAG-3' (SEQ ID NO: 863)

5'-ACCAAAAUCAUCUGUGCCCAGCAgt-3' (SEQ ID NO: 152)
3'-ACUGGUUUUAGUAGACACGGGUCGUCA-5' (SEQ ID NO: 508)

EGFR-901 Target: 5'-TGACCAAAATCATCTGTGCCCAGCAGT-3' (SEQ ID NO: 864)

5'-CCAAAUCAUCUGUGCCCAGCAGtg-3' (SEQ ID NO: 153)
3'-CUGGUUUUAGUAGACACGGGUCGUCAC-5' (SEQ ID NO: 509)

EGFR-902 Target: 5'-GACCAAAATCATCTGTGCCCAGCAGTG-3' (SEQ ID NO: 865)

5'-CAAAAUCAUCUGUGCCCAGCAGUgc-3' (SEQ ID NO: 154)
3'-UGGUUUUAGUAGACACGGGUCGUCACG-5' (SEQ ID NO: 510)

EGFR-903 Target: 5'-ACCAAAATCATCTGTGCCCAGCAGTGC-3' (SEQ ID NO: 866)

5'-AAAAUCAUCUGUGCCCAGCAGUGct-3' (SEQ ID NO: 155)
3'-GGUUUUAGUAGACACGGGUCGUCACGA-5' (SEQ ID NO: 511)

EGFR-904 Target: 5'-CCAAATCATCTGTGCCCAGCAGTGCT-3' (SEQ ID NO: 867)

5'-AAAUCAUCUGUGCCCAGCAGUGCtc-3' (SEQ ID NO: 156)
3'-GUUUUAGUAGACACGGGUCGUCACGAG-5' (SEQ ID NO: 512)

EGFR-905 Target: 5'-CAAAATCATCTGTGCCCAGCAGTGCTC-3' (SEQ ID NO: 868)

5'-CAGUGACUGCUGCCACAACCAGUgt-3' (SEQ ID NO: 157)
3'-GGGUCACUGACGACGGUGUUGGUCACA-5' (SEQ ID NO: 513)

EGFR-954 Target: 5'-CCCAGTGACTGCTGCCACAACCAGTGT-3' (SEQ ID NO: 869)

5'-AGUGACUGCUGCCACAACCAGUGtg-3' (SEQ ID NO: 158)
3'-GGUCACUGACGACGGUGUUGGUCACAC-5' (SEQ ID NO: 514)

EGFR-955 Target: 5'-CCAGTGACTGCTGCCACAACCAGTGTG-3' (SEQ ID NO: 870)

5'-GUGACUGCUGCCACAACCAGUGUgc-3' (SEQ ID NO: 159)
3'-GUCACUGACGACGGUGUUGGUCACACG-5' (SEQ ID NO: 515)

EGFR-956 Target: 5'-CAGTGACTGCTGCCACAACCAGTGTGC-3' (SEQ ID NO: 871)

5'-CACUCUCCAUAUAAUGCUACGAUat-3' (SEQ ID NO: 160)
3'-GAGUGAGAGGUAAUUACGAUGCUUAUA-5' (SEQ ID NO: 516)

EGFR-1313 Target: 5'-CTCACTCTCCATAAATGCTACGAATAT-3' (SEQ ID NO: 872)

5'-UUUUUGCUGAUUCAGGCUUGGCCtg-3' (SEQ ID NO: 161)
3'-CCAAAAACGACUAAGUCCGAACCGGAC-5' (SEQ ID NO: 517)

EGFR-1480 Target: 5'-GGTTTTTGCTGATTTCAGGCTTGGCCTG-3' (SEQ ID NO: 873)

5'-UUUUGCUGAUUCAGGCUUGGCCUga-3' (SEQ ID NO: 162)
3'-CAAAAACGACUAAGUCCGAACCGGACU-5' (SEQ ID NO: 518)

EGFR-1481 Target: 5'-GTTTTTGCTGATTTCAGGCTTGGCCTGA-3' (SEQ ID NO: 874)

5'-UUUGCUGAUUCAGGCUUGGCCUGaa-3' (SEQ ID NO: 163)

3'-AAAAACGACUAAGUCCGAACCGGACUU-5' (SEQ ID NO: 519)
EGFR-1482 Target: 5'-TTTTTGCTGATTTCAGGCTTGGCCTGAA-3' (SEQ ID NO: 875)

5'-UUGCUGAUUCAGGCUUGGCCUGAAa-3' (SEQ ID NO: 164)
3'-AAAACGACUAAGUCCGAACCGGACUUU-5' (SEQ ID NO: 520)
EGFR-1483 Target: 5'-TTTTGCTGATTTCAGGCTTGGCCTGAAA-3' (SEQ ID NO: 876)

5'-UGCUGAUUCAGGCUUGGCCUGAAaa-3' (SEQ ID NO: 165)
3'-AAACGACUAAGUCCGAACCGGACUUUU-5' (SEQ ID NO: 521)
EGFR-1484 Target: 5'-TTTGCTGATTTCAGGCTTGGCCTGAAAA-3' (SEQ ID NO: 877)

5'-GCUGAUUCAGGCUUGGCCUGAAAac-3' (SEQ ID NO: 166)
3'-AACGACUAAGUCCGAACCGGACUUUUG-5' (SEQ ID NO: 522)
EGFR-1485 Target: 5'-TTGCTGATTTCAGGCTTGGCCTGAAAAC-3' (SEQ ID NO: 878)

5'-CUGAUUCAGGCUUGGCCUGAAAAca-3' (SEQ ID NO: 167)
3'-ACGACUAAGUCCGAACCGGACUUUUGU-5' (SEQ ID NO: 523)
EGFR-1486 Target: 5'-TGCTGATTTCAGGCTTGGCCTGAAAACA-3' (SEQ ID NO: 879)

5'-UGAUUCAGGCUUGGCCUGAAAACag-3' (SEQ ID NO: 168)
3'-CGACUAAGUCCGAACCGGACUUUUGUC-5' (SEQ ID NO: 524)
EGFR-1487 Target: 5'-GCTGATTTCAGGCTTGGCCTGAAAACAG-3' (SEQ ID NO: 880)

5'-AAGCAACAUGGUCAGUUUUCUCUtg-3' (SEQ ID NO: 169)
3'-GGUUCGUUGUACCAGUCAAAAAGAGAAC-5' (SEQ ID NO: 525)
EGFR-1561 Target: 5'-CCAAGCAACATGGTCAGTTTTCTCTTG-3' (SEQ ID NO: 881)

5'-AGCAACAUGGUCAGUUUUCUCUUgc-3' (SEQ ID NO: 170)
3'-GUUCGUUGUACCAGUCAAAAAGAGAACG-5' (SEQ ID NO: 526)
EGFR-1562 Target: 5'-CAAGCAACATGGTCAGTTTTCTCTTGC-3' (SEQ ID NO: 882)

5'-GCAACAUGGUCAGUUUUCUCUUGca-3' (SEQ ID NO: 171)
3'-UUCGUUGUACCAGUCAAAAAGAGAACGU-5' (SEQ ID NO: 527)
EGFR-1563 Target: 5'-AAGCAACATGGTCAGTTTTCTCTTGCA-3' (SEQ ID NO: 883)

5'-CAAUAAACUGGAAAAAACUGUUUgg-3' (SEQ ID NO: 172)
3'-AUGUUAUUUGACCUUUUUUGACAAACC-5' (SEQ ID NO: 528)
EGFR-1691 Target: 5'-TACAATAAACTGGAAAAAACTGTTTGG-3' (SEQ ID NO: 884)

5'-CAGGCCAUGAACAUCACCUGCACag-3' (SEQ ID NO: 173)
3'-GAGUCCGGUACUUGUAGUGGACGUGUC-5' (SEQ ID NO: 529)
EGFR-1963 Target: 5'-CTCAGGCCATGAACATCACCTGCACAG-3' (SEQ ID NO: 885)

5'-AGGCCAUGAACAUCACCUGCACAgg-3' (SEQ ID NO: 174)
3'-AGUCCGGUACUUGUAGUGGACGUGUCC-5' (SEQ ID NO: 530)
EGFR-1964 Target: 5'-TCAGGCCATGAACATCACCTGCACAGG-3' (SEQ ID NO: 886)

5'-AUCCAGUGUGCCCACUACAUUGACg-3' (SEQ ID NO: 175)
 3'-CAUAGGUCACACGGGUGAUGUAACUGC-5' (SEQ ID NO: 531)
 EGFR-2008 Target: 5'-GTATCCAGTGTGCCCCACTACATTGACG-3' (SEQ ID NO: 887)

5'-UCCAGUGUGCCCACUACAUUGACgg-3' (SEQ ID NO: 176)
 3'-AUAGGUCACACGGGUGAUGUAACUGCC-5' (SEQ ID NO: 532)
 EGFR-2009 Target: 5'-TATCCAGTGTGCCCCACTACATTGACGG-3' (SEQ ID NO: 888)

5'-CCAGUGUGCCCACUACAUUGACGgc-3' (SEQ ID NO: 177)
 3'-UAGGUCACACGGGUGAUGUAACUGCCG-5' (SEQ ID NO: 533)
 EGFR-2010 Target: 5'-ATCCAGTGTGCCCCACTACATTGACGGC-3' (SEQ ID NO: 889)

5'-CAGUGUGCCCACUACAUUGACGGcc-3' (SEQ ID NO: 178)
 3'-AGGUCACACGGGUGAUGUAACUGCCGG-5' (SEQ ID NO: 534)
 EGFR-2011 Target: 5'-TCCAGTGTGCCCCACTACATTGACGGCC-3' (SEQ ID NO: 890)

5'-AGUGUGCCCACUACAUUGACGGCcc-3' (SEQ ID NO: 179)
 3'-GGUCACACGGGUGAUGUAACUGCCGGG-5' (SEQ ID NO: 535)
 EGFR-2012 Target: 5'-CCAGTGTGCCCCACTACATTGACGGCCC-3' (SEQ ID NO: 891)

5'-GAAUUCAAAAAGAUCAAAGUGCUgg-3' (SEQ ID NO: 180)
 3'-GACUUAAGUUUUUCUAGUUUCACGACC-5' (SEQ ID NO: 536)
 EGFR-2401 Target: 5'-CTGAATTCAAAAAGATCAAAGTGCTGG-3' (SEQ ID NO: 892)

5'-AAUUCAAAAAGAUCAAAGUGCUGgg-3' (SEQ ID NO: 181)
 3'-ACUUAAGUUUUUCUAGUUUCACGACCC-5' (SEQ ID NO: 537)
 EGFR-2402 Target: 5'-TGAATTCAAAAAGATCAAAGTGCTGGG-3' (SEQ ID NO: 893)

5'-CUCUGGAUCCCAGAAGGUGAGAAag-3' (SEQ ID NO: 182)
 3'-CUGAGACCUAGGGUCUCCACUCUUUC-5' (SEQ ID NO: 538)
 EGFR-2458 Target: 5'-GACTCTGGATCCCAGAAGGTGAGAAAG-3' (SEQ ID NO: 894)

5'-UCUGGAUCCCAGAAGGUGAGAAAgt-3' (SEQ ID NO: 183)
 3'-UGAGACCUAGGGUCUCCACUCUUUCA-5' (SEQ ID NO: 539)
 EGFR-2459 Target: 5'-ACTCTGGATCCCAGAAGGTGAGAAAGT-3' (SEQ ID NO: 895)

5'-CUGGAUCCCAGAAGGUGAGAAAGtt-3' (SEQ ID NO: 184)
 3'-GAGACCUAGGGUCUCCACUCUUUCA-5' (SEQ ID NO: 540)
 EGFR-2460 Target: 5'-CTCTGGATCCCAGAAGGTGAGAAAGTT-3' (SEQ ID NO: 896)

5'-UGGAUCCCAGAAGGUGAGAAAGUta-3' (SEQ ID NO: 185)
 3'-AGACCUAGGGUCUCCACUCUUUCAAU-5' (SEQ ID NO: 541)
 EGFR-2461 Target: 5'-TCTGGATCCCAGAAGGTGAGAAAGTTA-3' (SEQ ID NO: 897)

5'-GGAUCCCAGAAGGUGAGAAAGUUaa-3' (SEQ ID NO: 186)
 3'-GACCUAGGGUCUCCACUCUUUCAAUU-5' (SEQ ID NO: 542)
 EGFR-2462 Target: 5'-CTGGATCCCAGAAGGTGAGAAAGTTAA-3' (SEQ ID NO: 898)

5'-GAUCCCAGAAGGUGAGAAAGUUAaa-3' (SEQ ID NO: 187)
3'-ACCUAGGGUCUCCACUCUUUCAUUU-5' (SEQ ID NO: 543)
EGFR-2463 Target: 5'-TGGATCCCAGAAGGTGAGAAAGTTAAA-3' (SEQ ID NO: 899)

5'-AUCCCAGAAGGUGAGAAAGUUAaa-3' (SEQ ID NO: 188)
3'-CCUAGGGUCUCCACUCUUUCAUUU-5' (SEQ ID NO: 544)
EGFR-2464 Target: 5'-GGATCCCAGAAGGTGAGAAAGTTAAAA-3' (SEQ ID NO: 900)

5'-UCCCAGAAGGUGAGAAAGUUAaa-3' (SEQ ID NO: 189)
3'-CUAGGGUCUCCACUCUUUCAUUUA-5' (SEQ ID NO: 545)
EGFR-2465 Target: 5'-GATCCCAGAAGGTGAGAAAGTTAAAAT-3' (SEQ ID NO: 901)

5'-CAGCAUGUCAAGAUCACAGAUUUtg-3' (SEQ ID NO: 190)
3'-GCGUCGUACAGUUCUAGUGUCUAAAAC-5' (SEQ ID NO: 546)
EGFR-2815 Target: 5'-CGCAGCATGTCAAGATCACAGATTTTG-3' (SEQ ID NO: 902)

5'-AGCAUGUCAAGAUCACAGAUUUUgg-3' (SEQ ID NO: 191)
3'-CGUCGUACAGUUCUAGUGUCUAAAACC-5' (SEQ ID NO: 547)
EGFR-2816 Target: 5'-GCAGCATGTCAAGATCACAGATTTTGG-3' (SEQ ID NO: 903)

5'-GCAUGUCAAGAUCACAGAUUUUGg-3' (SEQ ID NO: 192)
3'-GUCGUACAGUUCUAGUGUCUAAAACCC-5' (SEQ ID NO: 548)
EGFR-2817 Target: 5'-CAGCATGTCAAGATCACAGATTTTGGG-3' (SEQ ID NO: 904)

5'-CAUGUCAAGAUCACAGAUUUUGGgc-3' (SEQ ID NO: 193)
3'-UCGUACAGUUCUAGUGUCUAAAACCCG-5' (SEQ ID NO: 549)
EGFR-2818 Target: 5'-AGCATGTCAAGATCACAGATTTTGGGC-3' (SEQ ID NO: 905)

5'-AUGUCAAGAUCACAGAUUUUGGGct-3' (SEQ ID NO: 194)
3'-CGUACAGUUCUAGUGUCUAAAACCCGA-5' (SEQ ID NO: 550)
EGFR-2819 Target: 5'-GCATGTCAAGATCACAGATTTTGGGCT-3' (SEQ ID NO: 906)

5'-UGUCAAGAUCACAGAUUUUGGGCtg-3' (SEQ ID NO: 195)
3'-GUACAGUUCUAGUGUCUAAAACCCGAC-5' (SEQ ID NO: 551)
EGFR-2820 Target: 5'-CATGTCAAGATCACAGATTTTGGGCTG-3' (SEQ ID NO: 907)

5'-GUCAAGAUCACAGAUUUUGGGCUgg-3' (SEQ ID NO: 196)
3'-UACAGUUCUAGUGUCUAAAACCCGACC-5' (SEQ ID NO: 552)
EGFR-2821 Target: 5'-ATGTCAAGATCACAGATTTTGGGCTGG-3' (SEQ ID NO: 908)

5'-UCAAGAUCACAGAUUUUGGGCUGgc-3' (SEQ ID NO: 197)
3'-ACAGUUCUAGUGUCUAAAACCCGACCG-5' (SEQ ID NO: 553)
EGFR-2822 Target: 5'-TGTCAAGATCACAGATTTTGGGCTGGC-3' (SEQ ID NO: 909)

5'-CAAGAUCACAGAUUUUGGGCUGGcc-3' (SEQ ID NO: 198)
3'-CAGUUCUAGUGUCUAAAACCCGACCGG-5' (SEQ ID NO: 554)

EGFR-2823 Target: 5'-GTCAAGATCACAGATTTTGGGCTGGCC-3' (SEQ ID NO: 910)

5'-AAGAUCACAGAUUUUGGGCUGGCCa-3' (SEQ ID NO: 199)

3'-AGUUCUAGUGUCUAAAACCCGACCGGU-5' (SEQ ID NO: 555)

EGFR-2824 Target: 5'-TCAAGATCACAGATTTTGGGCTGGCCA-3' (SEQ ID NO: 911)

5'-AGAUCACAGAUUUUGGGCUGGCCa-3' (SEQ ID NO: 200)

3'-GUUCUAGUGUCUAAAACCCGACCGGUU-5' (SEQ ID NO: 556)

EGFR-2825 Target: 5'-CAAGATCACAGATTTTGGGCTGGCCAA-3' (SEQ ID NO: 912)

5'-GAUCACAGAUUUUGGGCUGGCCAa-3' (SEQ ID NO: 201)

3'-UUCUAGUGUCUAAAACCCGACCGGUU-5' (SEQ ID NO: 557)

EGFR-2826 Target: 5'-AAGATCACAGATTTTGGGCTGGCCAAA-3' (SEQ ID NO: 913)

5'-AUCACAGAUUUUGGGCUGGCCAAac-3' (SEQ ID NO: 202)

3'-UCUAGUGUCUAAAACCCGACCGGUUUG-5' (SEQ ID NO: 558)

EGFR-2827 Target: 5'-AGATCACAGATTTTGGGCTGGCCAAAC-3' (SEQ ID NO: 914)

5'-UCACAGAUUUUGGGCUGGCCAAAAct-3' (SEQ ID NO: 203)

3'-CUAGUGUCUAAAACCCGACCGGUUUGA-5' (SEQ ID NO: 559)

EGFR-2828 Target: 5'-GATCACAGATTTTGGGCTGGCCAAACT-3' (SEQ ID NO: 915)

5'-CACAGAUUUUGGGCUGGCCAAACTg-3' (SEQ ID NO: 204)

3'-UAGUGUCUAAAACCCGACCGGUUUGAC-5' (SEQ ID NO: 560)

EGFR-2829 Target: 5'-ATCACAGATTTTGGGCTGGCCAAACTG-3' (SEQ ID NO: 916)

5'-ACAGAUUUUGGGCUGGCCAAACUgc-3' (SEQ ID NO: 205)

3'-AGUGUCUAAAACCCGACCGGUUUGACG-5' (SEQ ID NO: 561)

EGFR-2830 Target: 5'-TCACAGATTTTGGGCTGGCCAAACTGC-3' (SEQ ID NO: 917)

5'-CAGAUUUUGGGCUGGCCAAACUGct-3' (SEQ ID NO: 206)

3'-GUGUCUAAAACCCGACCGGUUUGACGA-5' (SEQ ID NO: 562)

EGFR-2831 Target: 5'-CACAGATTTTGGGCTGGCCAAACTGCT-3' (SEQ ID NO: 918)

5'-AGAUUUUGGGCUGGCCAAACUGCtg-3' (SEQ ID NO: 207)

3'-UGUCUAAAACCCGACCGGUUUGACGAC-5' (SEQ ID NO: 563)

EGFR-2832 Target: 5'-ACAGATTTTGGGCTGGCCAAACTGCTG-3' (SEQ ID NO: 919)

5'-GAUUUUGGGCUGGCCAAACUGCUgg-3' (SEQ ID NO: 208)

3'-GUCUAAAACCCGACCGGUUUGACGACC-5' (SEQ ID NO: 564)

EGFR-2833 Target: 5'-CAGATTTTGGGCTGGCCAAACTGCTGG-3' (SEQ ID NO: 920)

5'-AUUUUGGGCUGGCCAAACUGCUGgg-3' (SEQ ID NO: 209)

3'-UCUAAAACCCGACCGGUUUGACGACCC-5' (SEQ ID NO: 565)

EGFR-2834 Target: 5'-AGATTTTGGGCTGGCCAAACTGCTGGG-3' (SEQ ID NO: 921)

5'-UUUUGGGCUGGCCAAACUGCUGGgt-3' (SEQ ID NO: 210)

3'-CUAAAACCCGACCGGUUUGACGACCCA-5' (SEQ ID NO: 566)
 EGFR-2835 Target: 5'-GATTTTGGGCTGGCCAAACTGCTGGGT-3' (SEQ ID NO: 922)

5'-UUUGGGCUGGCCAAACUGCUGGGtg-3' (SEQ ID NO: 211)
 3'-UAAAACCCGACCGGUUUGACGACCCAC-5' (SEQ ID NO: 567)
 EGFR-2836 Target: 5'-ATTTTGGGCTGGCCAAACTGCTGGGTG-3' (SEQ ID NO: 923)

5'-UUGGGCUGGCCAAACUGCUGGGUgc-3' (SEQ ID NO: 212)
 3'-AAAACCCGACCGGUUUGACGACCCACG-5' (SEQ ID NO: 568)
 EGFR-2837 Target: 5'-TTTTGGGCTGGCCAAACTGCTGGGTGC-3' (SEQ ID NO: 924)

5'-GCAAAGUGCCUAUCAAGUGGAUGgc-3' (SEQ ID NO: 213)
 3'-UCCGUUUCACGGAUAGUUCACCUACCG-5' (SEQ ID NO: 569)
 EGFR-2891 Target: 5'-AGGCAAAGTGCCTATCAAGTGGATGGC-3' (SEQ ID NO: 925)

5'-CAAAGUGCCUAUCAAGUGGAUGGca-3' (SEQ ID NO: 214)
 3'-CCGUUUCACGGAUAGUUCACCUACCGU-5' (SEQ ID NO: 570)
 EGFR-2892 Target: 5'-GGCAAAGTGCCTATCAAGTGGATGGCA-3' (SEQ ID NO: 926)

5'-AAAGUGCCUAUCAAGUGGAUGGCat-3' (SEQ ID NO: 215)
 3'-CGUUUCACGGAUAGUUCACCUACCGUA-5' (SEQ ID NO: 571)
 EGFR-2893 Target: 5'-GCAAAGTGCCTATCAAGTGGATGGCAT-3' (SEQ ID NO: 927)

5'-AAGUGCCUAUCAAGUGGAUGGCAtt-3' (SEQ ID NO: 216)
 3'-GUUUCACGGAUAGUUCACCUACCGUAA-5' (SEQ ID NO: 572)
 EGFR-2894 Target: 5'-CAAAGTGCCTATCAAGTGGATGGCATT-3' (SEQ ID NO: 928)

5'-AGUGCCUAUCAAGUGGAUGGCAUtg-3' (SEQ ID NO: 217)
 3'-UUUCACGGAUAGUUCACCUACCGUAAC-5' (SEQ ID NO: 573)
 EGFR-2895 Target: 5'-AAAGTGCCTATCAAGTGGATGGCATTG-3' (SEQ ID NO: 929)

5'-GUGCCUAUCAAGUGGAUGGCAUUgg-3' (SEQ ID NO: 218)
 3'-UUCACGGAUAGUUCACCUACCGUAACC-5' (SEQ ID NO: 574)
 EGFR-2896 Target: 5'-AAGTGCCTATCAAGTGGATGGCATTGG-3' (SEQ ID NO: 930)

5'-UGCCUAUCAAGUGGAUGGCAUUGga-3' (SEQ ID NO: 219)
 3'-UCACGGAUAGUUCACCUACCGUAACCU-5' (SEQ ID NO: 575)
 EGFR-2897 Target: 5'-AGTGCCTATCAAGTGGATGGCATTGGA-3' (SEQ ID NO: 931)

5'-ACCAUCGAUGUCUACAUGAUCAUgg-3' (SEQ ID NO: 220)
 3'-CAUGGUAGCUACAGAUGUACUAGUACC-5' (SEQ ID NO: 576)
 EGFR-3088 Target: 5'-GTACCATCGATGTCTACATGATCATGG-3' (SEQ ID NO: 932)

5'-CCAUCGAUGUCUACAUGAUCAUGgt-3' (SEQ ID NO: 221)
 3'-AUGGUAGCUACAGAUGUACUAGUACCA-5' (SEQ ID NO: 577)
 EGFR-3089 Target: 5'-TACCATCGATGTCTACATGATCATGGT-3' (SEQ ID NO: 933)

5'-CAUCGAUGUCUACAUGAUGGtc-3' (SEQ ID NO: 222)
3'-UGGUAGCUACAGAUGUACUAGUACCAG-5' (SEQ ID NO: 578)
EGFR-3090 Target: 5'-ACCATCGATGTCTACATGATCATGGTC-3' (SEQ ID NO: 934)

5'-AUCGAUGUCUACAUGAUGGUca-3' (SEQ ID NO: 223)
3'-GGUAGCUACAGAUGUACUAGUACCAGU-5' (SEQ ID NO: 579)
EGFR-3091 Target: 5'-CCATCGATGTCTACATGATCATGGTCA-3' (SEQ ID NO: 935)

5'-UCGAUGUCUACAUGAUGGUCaa-3' (SEQ ID NO: 224)
3'-GUAGCUACAGAUGUACUAGUACCAGUU-5' (SEQ ID NO: 580)
EGFR-3092 Target: 5'-CATCGATGTCTACATGATCATGGTCAA-3' (SEQ ID NO: 936)

5'-CGAUGUCUACAUGAUGGUCAag-3' (SEQ ID NO: 225)
3'-UAGCUACAGAUGUACUAGUACCAGUUC-5' (SEQ ID NO: 581)
EGFR-3093 Target: 5'-ATCGATGTCTACATGATCATGGTCAAG-3' (SEQ ID NO: 937)

5'-GAUGUCUACAUGAUGGUCAAgt-3' (SEQ ID NO: 226)
3'-AGCUACAGAUGUACUAGUACCAGUUCA-5' (SEQ ID NO: 582)
EGFR-3094 Target: 5'-TCGATGTCTACATGATCATGGTCAAGT-3' (SEQ ID NO: 938)

5'-AUGUCUACAUGAUGGUCAAGtg-3' (SEQ ID NO: 227)
3'-GCUACAGAUGUACUAGUACCAGUUCAC-5' (SEQ ID NO: 583)
EGFR-3095 Target: 5'-CGATGTCTACATGATCATGGTCAAGTG-3' (SEQ ID NO: 939)

5'-UGUCUACAUGAUGGUCAAGUgc-3' (SEQ ID NO: 228)
3'-CUACAGAUGUACUAGUACCAGUUCACG-5' (SEQ ID NO: 584)
EGFR-3096 Target: 5'-GATGTCTACATGATCATGGTCAAGTGC-3' (SEQ ID NO: 940)

5'-GUCUACAUGAUGGUCAAGUGct-3' (SEQ ID NO: 229)
3'-UACAGAUGUACUAGUACCAGUUCACGA-5' (SEQ ID NO: 585)
EGFR-3097 Target: 5'-ATGTCTACATGATCATGGTCAAGTGCT-3' (SEQ ID NO: 941)

5'-UCUACAUGAUGGUCAAGUGCtg-3' (SEQ ID NO: 230)
3'-ACAGAUGUACUAGUACCAGUUCACGAC-5' (SEQ ID NO: 586)
EGFR-3098 Target: 5'-TGTCTACATGATCATGGTCAAGTGCTG-3' (SEQ ID NO: 942)

5'-CUACAUGAUGGUCAAGUGCUgg-3' (SEQ ID NO: 231)
3'-CAGAUGUACUAGUACCAGUUCACGACC-5' (SEQ ID NO: 587)
EGFR-3099 Target: 5'-GTCTACATGATCATGGTCAAGTGCTGG-3' (SEQ ID NO: 943)

5'-UACAUGAUGGUCAAGUGCUGga-3' (SEQ ID NO: 232)
3'-AGAUGUACUAGUACCAGUUCACGACCU-5' (SEQ ID NO: 588)
EGFR-3100 Target: 5'-TCTACATGATCATGGTCAAGTGCTGGA-3' (SEQ ID NO: 944)

5'-ACAUGAUGGUCAAGUGCUGGat-3' (SEQ ID NO: 233)
3'-GAUGUACUAGUACCAGUUCACGACCUA-5' (SEQ ID NO: 589)
EGFR-3101 Target: 5'-CTACATGATCATGGTCAAGTGCTGGAT-3' (SEQ ID NO: 945)

5'-CAUGAUC AUGGUCAAGUGCUGGAtg-3' (SEQ ID NO: 234)
3'-AUGUACUAGUACCAGUUCACGACCUAC-5' (SEQ ID NO: 590)
EGFR-3102 Target: 5'-TACATGATCATGGTCAAGTGCTGGATG-3' (SEQ ID NO: 946)

5'-AUGAUC AUGGUCAAGUGCUGGAUga-3' (SEQ ID NO: 235)
3'-UGUACUAGUACCAGUUCACGACCUACU-5' (SEQ ID NO: 591)
EGFR-3103 Target: 5'-ACATGATCATGGTCAAGTGCTGGATGA-3' (SEQ ID NO: 947)

5'-UGAUC AUGGUCAAGUGCUGGAUGat-3' (SEQ ID NO: 236)
3'-GUACUAGUACCAGUUCACGACCUACUA-5' (SEQ ID NO: 592)
EGFR-3104 Target: 5'-CATGATCATGGTCAAGTGCTGGATGAT-3' (SEQ ID NO: 948)

5'-GAUC AUGGUCAAGUGCUGGAUGAta-3' (SEQ ID NO: 237)
3'-UACUAGUACCAGUUCACGACCUACUAU-5' (SEQ ID NO: 593)
EGFR-3105 Target: 5'-ATGATCATGGTCAAGTGCTGGATGATA-3' (SEQ ID NO: 949)

5'-AUC AUGGUCAAGUGCUGGAUGAUag-3' (SEQ ID NO: 238)
3'-ACUAGUACCAGUUCACGACCUACUAUC-5' (SEQ ID NO: 594)
EGFR-3106 Target: 5'-TGATCATGGTCAAGTGCTGGATGATAG-3' (SEQ ID NO: 950)

5'-UCAUGGUCAAGUGCUGGAUGAUAg-3' (SEQ ID NO: 239)
3'-CUAGUACCAGUUCACGACCUACUAUCU-5' (SEQ ID NO: 595)
EGFR-3107 Target: 5'-GATCATGGTCAAGTGCTGGATGATAGA-3' (SEQ ID NO: 951)

5'-CAUGGUCAAGUGCUGGAUGAUAGac-3' (SEQ ID NO: 240)
3'-UAGUACCAGUUCACGACCUACUAUCUG-5' (SEQ ID NO: 596)
EGFR-3108 Target: 5'-ATCATGGTCAAGTGCTGGATGATAGAC-3' (SEQ ID NO: 952)

5'-AUGGUCAAGUGCUGGAUGAUAGAcg-3' (SEQ ID NO: 241)
3'-AGUACCAGUUCACGACCUACUAUCUGC-5' (SEQ ID NO: 597)
EGFR-3109 Target: 5'-TCATGGTCAAGTGCTGGATGATAGACG-3' (SEQ ID NO: 953)

5'-UGGUCAAGUGCUGGAUGAUAGACGgc-3' (SEQ ID NO: 242)
3'-GUACCAGUUCACGACCUACUAUCUGCG-5' (SEQ ID NO: 598)
EGFR-3110 Target: 5'-CATGGTCAAGTGCTGGATGATAGACGC-3' (SEQ ID NO: 954)

5'-GGUCAAGUGCUGGAUGAUAGACGca-3' (SEQ ID NO: 243)
3'-UACCAGUUCACGACCUACUAUCUGCGU-5' (SEQ ID NO: 599)
EGFR-3111 Target: 5'-ATGGTCAAGTGCTGGATGATAGACGCA-3' (SEQ ID NO: 955)

5'-GUCAAGUGCUGGAUGAUAGACGCag-3' (SEQ ID NO: 244)
3'-ACCAGUUCACGACCUACUAUCUGCGUC-5' (SEQ ID NO: 600)
EGFR-3112 Target: 5'-TGGTCAAGTGCTGGATGATAGACGCAG-3' (SEQ ID NO: 956)

5'-UCAAGUGCUGGAUGAUAGACGCaga-3' (SEQ ID NO: 245)
3'-CCAGUUCACGACCUACUAUCUGCGUCU-5' (SEQ ID NO: 601)

EGFR-3113 Target: 5'-GGTCAAGTGCTGGATGATAGACGCAGA-3' (SEQ ID NO: 957)

5'-GAAUUCUCCAAAAUGGCCCCGAGAcc-3' (SEQ ID NO: 246)

3'-AGCUUAAGAGGUUUUACCGGGCUCUGG-5' (SEQ ID NO: 602)

EGFR-3169 Target: 5'-TCGAATTCTCCAAAATGGCCCCGAGACC-3' (SEQ ID NO: 958)

5'-AAUUCUCCAAAAUGGCCCCGAGACcc-3' (SEQ ID NO: 247)

3'-GCUUAAGAGGUUUUACCGGGCUCUGGG-5' (SEQ ID NO: 603)

EGFR-3170 Target: 5'-CGAATTCTCCAAAATGGCCCCGAGACCC-3' (SEQ ID NO: 959)

5'-GAUGAAAGAAUGCAUUUGCCAAGtc-3' (SEQ ID NO: 248)

3'-CCCUACUUUCUUACGUAAACGGUUCAG-5' (SEQ ID NO: 604)

EGFR-3220 Target: 5'-GGGATGAAAGAATGCATTTGCCAAGTC-3' (SEQ ID NO: 960)

5'-AUGAAAGAAUGCAUUUGCCAAGUcc-3' (SEQ ID NO: 249)

3'-CCUACUUUCUUACGUAAACGGUUCAGG-5' (SEQ ID NO: 605)

EGFR-3221 Target: 5'-GGATGAAAGAATGCATTTGCCAAGTCC-3' (SEQ ID NO: 961)

5'-UGAAAGAAUGCAUUUGCCAAGUCct-3' (SEQ ID NO: 250)

3'-CUACUUUCUUACGUAAACGGUUCAGGA-5' (SEQ ID NO: 606)

EGFR-3222 Target: 5'-GATGAAAGAATGCATTTGCCAAGTCCT-3' (SEQ ID NO: 962)

5'-GAAAGAAUGCAUUUGCCAAGUCCta-3' (SEQ ID NO: 251)

3'-UACUUUCUUACGUAAACGGUUCAGGAU-5' (SEQ ID NO: 607)

EGFR-3223 Target: 5'-ATGAAAGAATGCATTTGCCAAGTCCTA-3' (SEQ ID NO: 963)

5'-AAAGAAUGCAUUUGCCAAGUCCUac-3' (SEQ ID NO: 252)

3'-ACUUUUCUUACGUAAACGGUUCAGGAUG-5' (SEQ ID NO: 608)

EGFR-3224 Target: 5'-TGAAAGAATGCATTTGCCAAGTCCTAC-3' (SEQ ID NO: 964)

5'-GACAACCCUGACUACCAGCAGGAct-3' (SEQ ID NO: 253)

3'-ACCUGUUGGGACUGAUGGUCGUCCUGA-5' (SEQ ID NO: 609)

EGFR-3772 Target: 5'-TGGACAACCCTGACTACCAGCAGGACT-3' (SEQ ID NO: 965)

5'-ACAACCCUGACUACCAGCAGGACTt-3' (SEQ ID NO: 254)

3'-CCUGUUGGGACUGAUGGUCGUCCUGAA-5' (SEQ ID NO: 610)

EGFR-3773 Target: 5'-GGACAACCCTGACTACCAGCAGGACTT-3' (SEQ ID NO: 966)

5'-CAACCCUGACUACCAGCAGGACUtc-3' (SEQ ID NO: 255)

3'-CUGUUGGGACUGAUGGUCGUCCUGAAG-5' (SEQ ID NO: 611)

EGFR-3774 Target: 5'-GACAACCCTGACTACCAGCAGGACTTC-3' (SEQ ID NO: 967)

5'-AACCCUGACUACCAGCAGGACUUct-3' (SEQ ID NO: 256)

3'-UGUUUGGGACUGAUGGUCGUCCUGAAGA-5' (SEQ ID NO: 612)

EGFR-3775 Target: 5'-ACAACCCTGACTACCAGCAGGACTTCT-3' (SEQ ID NO: 968)

5'-ACCCUGACUACCAGCAGGACUUCtt-3' (SEQ ID NO: 257)

3'-GUUGGGACUGAUGGUCGUCCUGAAGAA-5' (SEQ ID NO: 613)
 EGFR-3776 Target: 5'-CAACCCTGACTACCAGCAGGACTTCTT-3' (SEQ ID NO: 969)

5'-CCCUGACUACCAGCAGGACUUCUtt-3' (SEQ ID NO: 258)
 3'-UUGGGACUGAUGGUCGUCCUGAAGAAA-5' (SEQ ID NO: 614)
 EGFR-3777 Target: 5'-AACCTGACTACCAGCAGGACTTCTTT-3' (SEQ ID NO: 970)

5'-CCUGACUACCAGCAGGACUUCUUt-3' (SEQ ID NO: 259)
 3'-UGGGACUGAUGGUCGUCCUGAAGAAAG-5' (SEQ ID NO: 615)
 EGFR-3778 Target: 5'-ACCCTGACTACCAGCAGGACTTCTTTC-3' (SEQ ID NO: 971)

5'-CUGACUACCAGCAGGACUUCUUUcc-3' (SEQ ID NO: 260)
 3'-GGGACUGAUGGUCGUCCUGAAGAAAGG-5' (SEQ ID NO: 616)
 EGFR-3779 Target: 5'-CCCTGACTACCAGCAGGACTTCTTTCC-3' (SEQ ID NO: 972)

Table 3: Selected Human Anti-EGFR DsiRNAs, Unmodified Duplexes (Asymmetrics)

5'-CGCAGCGCGGCCGCGAGCAGCCUCCG-3' (SEQ ID NO: 1069)
 3'-CCGCGUCGCGCCGGCGUCGUCGAGGC-5' (SEQ ID NO: 357)
 EGFR-31 Target: 5'-GGCGCAGCGCGGCCGCGAGCAGCCTCCG-3' (SEQ ID NO: 713)

5'-GCAGCGCGGCCGCGAGCAGCCUCCGC-3' (SEQ ID NO: 1070)
 3'-CGCGUCGCGCCGGCGUCGUCGAGGCG-5' (SEQ ID NO: 358)
 EGFR-32 Target: 5'-GCGCAGCGCGGCCGCGAGCAGCCTCCGC-3' (SEQ ID NO: 714)

5'-AGCGCGGCCGCGAGCAGCCUCCGCCC-3' (SEQ ID NO: 1071)
 3'-CGUCGCGCCGGCGUCGUCGAGGCGGG-5' (SEQ ID NO: 359)
 EGFR-34 Target: 5'-GCAGCGCGGCCGCGAGCAGCCTCCGCCC-3' (SEQ ID NO: 715)

5'-GCGCUCCUGGCGUGCUGGCUGCGC-3' (SEQ ID NO: 1072)
 3'-GUCGCGAGGACCGCGACGACCGACGCG-5' (SEQ ID NO: 360)
 EGFR-298 Target: 5'-CAGCGCTCCTGGCGCTGCTGGCTGCGC-3' (SEQ ID NO: 716)

5'-GCUCCUGGCGUGCUGGCUGCGCUC-3' (SEQ ID NO: 1073)
 3'-CGCGAGGACCGCGACGACCGACGCGAG-5' (SEQ ID NO: 361)
 EGFR-300 Target: 5'-GCGCTCCTGGCGCTGCTGGCTGCGCTC-3' (SEQ ID NO: 717)

5'-UCCUGGCGUGCUGGCUGCGCUCUG-3' (SEQ ID NO: 1074)
 3'-CGAGGACCGCGACGACCGACGCGAGAC-5' (SEQ ID NO: 362)
 EGFR-302 Target: 5'-GCTCCTGGCGCTGCTGGCTGCGCTCTG-3' (SEQ ID NO: 718)

5'-GUUGGGCACUUUUGAAGAUCAUUUU-3' (SEQ ID NO: 1075)
 3'-GUCAACCCGUGAAAACUUCUAGUAAAA-5' (SEQ ID NO: 363)
 EGFR-390 Target: 5'-CAGTTGGGCACTTTTGAAGATCATTTT-3' (SEQ ID NO: 719)

5'-GGAAUUUGGAAAUUACCUAUGUGCA-3' (SEQ ID NO: 1076)
 3'-ACCCUUAACCUUUAUGGAUACACGU-5' (SEQ ID NO: 364)

EGFR-458 Target: 5'-TGGGAATTTGGAAATTACCTATGTGCA-3' (SEQ ID NO: 720)

5'-UUAUGAUCUUUCCUUCUUAAGACC-3' (SEQ ID NO: 1077)

3'-UUAUACUAGAAAGGAAGAAUUUCUGG-5' (SEQ ID NO: 365)

EGFR-489 Target: 5'-AATTATGATCTTTCTTCTTAAAGACC-3' (SEQ ID NO: 721)

5'-GGCUGGUUAUGUCCUCAUUGCCCUC-3' (SEQ ID NO: 1078)

3'-CACCGACCAUACAGGAGUAACGGGAG-5' (SEQ ID NO: 366)

EGFR-525 Target: 5'-GTGGCTGGTTATGTCTCATTTGCCCTC-3' (SEQ ID NO: 722)

5'-CCCAUGAGAAAUUUACAGGAAAUCC-3' (SEQ ID NO: 1079)

3'-ACGGGUACUCUUUAAUGUCCUUUAGG-5' (SEQ ID NO: 367)

EGFR-676 Target: 5'-TGCCCATGAGAAATTTACAGGAAATCC-3' (SEQ ID NO: 723)

5'-UGCAUGGCGCCGUGCGGUUCAGCAA-3' (SEQ ID NO: 1080)

3'-GGACGUACCGCGGCACGCCAAGUCGUU-5' (SEQ ID NO: 368)

EGFR-701 Target: 5'-CCTGCATGGCGCCGTGCGGTTTACAGCAA-3' (SEQ ID NO: 724)

5'-GCGCCGUGCGGUUCAGCAACAACCC-3' (SEQ ID NO: 1081)

3'-ACCGCGGCACGCCAAGUCGUUGUUGGG-5' (SEQ ID NO: 369)

EGFR-707 Target: 5'-TGGCGCCGTGCGGTTTACAGCAACAACCC-3' (SEQ ID NO: 725)

5'-GCGCCGUGCGGUUCAGCAACAACCC-3' (SEQ ID NO: 1082)

3'-ACCGCGGCACGCCAAGUCGUUGUUGGG-5' (SEQ ID NO: 370)

EGFR-707 Target: 5'-TGGCGCCGTGCGGTTTACAGCAACAACCC-3' (SEQ ID NO: 726)

5'-GCCGUGCGGUUCAGCAACAACCCUG-3' (SEQ ID NO: 1083)

3'-CGCGGCACGCCAAGUCGUUGUUGGGAC-5' (SEQ ID NO: 371)

EGFR-709 Target: 5'-GCGCCGTGCGGTTTACAGCAACAACCCTG-3' (SEQ ID NO: 727)

5'-CCGUGCGGUUCAGCAACAACCCUGC-3' (SEQ ID NO: 1084)

3'-GCGGCACGCCAAGUCGUUGUUGGGACG-5' (SEQ ID NO: 372)

EGFR-710 Target: 5'-CGCCGTGCGGTTTACAGCAACAACCCTGC-3' (SEQ ID NO: 728)

5'-GCUGCCAAAAGUGUGAUCCAAGCUG-3' (SEQ ID NO: 1085)

3'-GUCGACGGUUUUCACACUAGGUUCGAC-5' (SEQ ID NO: 373)

EGFR-827 Target: 5'-CAGCTGCCAAAAGTGTGATCCAAGCTG-3' (SEQ ID NO: 729)

5'-CUGUGCCCAGCAGUGCUCCGGGCGC-3' (SEQ ID NO: 1086)

3'-UAGACACGGGUCGUCACGAGGCCCGCG-5' (SEQ ID NO: 374)

EGFR-912 Target: 5'-ATCTGTGCCCAGCAGTGCTCCGGGCGC-3' (SEQ ID NO: 730)

5'-GUGCCCAGCAGUGCUCCGGGCGCUG-3' (SEQ ID NO: 1087)

3'-GACACGGGUCGUCACGAGGCCCGCGAC-5' (SEQ ID NO: 375)

EGFR-914 Target: 5'-CTGTGCCCAGCAGTGCTCCGGGCGCTG-3' (SEQ ID NO: 731)

5'-GCUCCGGGCGCUGCCGUGGCAAGUC-3' (SEQ ID NO: 1088)

3'-CACGAGGCCCGCGACGGCACCGUUCAG-5' (SEQ ID NO: 376)
EGFR-926 Target: 5'-GTGCTCCGGGCGCTGCCGTGGCAAGTC-3' (SEQ ID NO: 732)

5'-GAGCGACUGCCUGGUCUGCCGCAA-3' (SEQ ID NO: 1089)
3'-CUCUCGCGACGGACCAGACGGCGUUU-5' (SEQ ID NO: 377)
EGFR-1005 Target: 5'-GAGAGCGACTGCCTGGTCTGCCGCAA-3' (SEQ ID NO: 733)

5'-GCCUGGUCUGCCGCAAUUCGAGA-3' (SEQ ID NO: 1090)
3'-GACGGACCAGACGGCGUUUAAGGCUCU-5' (SEQ ID NO: 378)
EGFR-1013 Target: 5'-CTGCCTGGTCTGCCGCAAATTCGAGA-3' (SEQ ID NO: 734)

5'-CAGAUACGGCUCGUGCGUCCGAGC-3' (SEQ ID NO: 1091)
3'-CUGUCUAGUGCCGAGCACGCAGGCUCG-5' (SEQ ID NO: 379)
EGFR-1175 Target: 5'-GACAGATCACGGCTCGTGCTCCGAGC-3' (SEQ ID NO: 735)

5'-GCAAAGUGUGUAAACGGAAUAGGUAAU-3' (SEQ ID NO: 1092)
3'-GGCGUUUCACACAUUGCCUUAUCCAUA-5' (SEQ ID NO: 380)
EGFR-1271 Target: 5'-CCGCAAAGTGTGTAACGGAATAGGTAT-3' (SEQ ID NO: 736)

5'-GAAUAGGUAAUUGGUGAAUUUAAAGA-3' (SEQ ID NO: 1093)
3'-GCCUUAUCCAUAACCACUUAUUUUUCU-5' (SEQ ID NO: 381)
EGFR-1286 Target: 5'-CGGAATAGGTATTGGTGAATTTAAAGA-3' (SEQ ID NO: 737)

5'-ACGAAUAUUAAACACUUCAAAAACU-3' (SEQ ID NO: 1094)
3'-GAUGC UUAUUUUUGUGAAGUUUUUGA-5' (SEQ ID NO: 382)
EGFR-1330 Target: 5'-CTACGAATATTAAACACTTCAAAAACT-3' (SEQ ID NO: 738)

5'-ACAGGAACUGGAUAUUCUGAAAACC-3' (SEQ ID NO: 1095)
3'-GGUGUCCUUGACCUAUAAGACUUUUGG-5' (SEQ ID NO: 383)
EGFR-1437 Target: 5'-CCACAGGAACTGGATATTCTGAAAACC-3' (SEQ ID NO: 739)

5'-CAGGGUUUUUGCUGAUUCAGGCUUG-3' (SEQ ID NO: 1096)
3'-GUGUCCCAAAAACGACUAAGUCCGAAC-5' (SEQ ID NO: 384)
EGFR-1475 Target: 5'-CACAGGGTTTTTGCTGATTCAGGCTTG-3' (SEQ ID NO: 740)

5'-CAGGAAACAAAAUUUGUGCUAUGC-3' (SEQ ID NO: 1097)
3'-AAGUCCUUUGUUUUUAAACACGAUACG-5' (SEQ ID NO: 385)
EGFR-1661 Target: 5'-TTCAGGAAACAAAAATTTGTGCTATGC-3' (SEQ ID NO: 741)

5'-GCUAUGCAAAUACAAUAAACUGGAA-3' (SEQ ID NO: 1098)
3'-CACGAUACGUUUAUGUUAUUUGACCUU-5' (SEQ ID NO: 386)
EGFR-1679 Target: 5'-GTGCTATGCAAATACAATAAACTGGAA-3' (SEQ ID NO: 742)

5'-GGUCAGAAAACCAAAUUAUAAGCA-3' (SEQ ID NO: 1099)
3'-GGCCAGUCUUUUGGUUUUAUAUUCGU-5' (SEQ ID NO: 387)
EGFR-1723 Target: 5'-CCGGTCAGAAAACCAAAATTATAAGCA-3' (SEQ ID NO: 743)

5'-GCGUCUCUUGCCGGA AUGUCAGCCG-3' (SEQ ID NO: 1100)
3'-GACGCAGAGAACGGCCUACAGUCGGC-5' (SEQ ID NO: 388)
EGFR-1838 Target: 5'-CTGCGTCTCTTGCCGGAATGTCAGCCG-3' (SEQ ID NO: 744)

5'-GCCCCUCCUCUUGCUGCUGGUGGUGG-3' (SEQ ID NO: 1101)
3'-CCCGGGAGGAGAACGACGACCACCACC-5' (SEQ ID NO: 389)
EGFR-2227 Target: 5'-GGGCCCTCCTCTTGCTGCTGGTGGTGG-3' (SEQ ID NO: 745)

5'-CCCUCCUCUUGCUGCUGGUGGUGG-3' (SEQ ID NO: 1102)
3'-CCGGGAGGAGAACGACGACCACCACCG-5' (SEQ ID NO: 390)
EGFR-2228 Target: 5'-GGCCCTCCTCTTGCTGCTGGTGGTGGC-3' (SEQ ID NO: 746)

5'-CCUCUUGCUGCUGGUGGUGGCCCCUG-3' (SEQ ID NO: 1103)
3'-GAGGAGAACGACGACCACCACCGGGAC-5' (SEQ ID NO: 391)
EGFR-2232 Target: 5'-CTCCTCTTGCTGCTGGTGGTGGCCCTG-3' (SEQ ID NO: 747)

5'-CUCUUGCUGCUGGUGGUGGCCCCUGG-3' (SEQ ID NO: 1104)
3'-AGGAGAACGACGACCACCACCGGGACC-5' (SEQ ID NO: 392)
EGFR-2233 Target: 5'-TCCTCTTGCTGCTGGTGGTGGCCCTGG-3' (SEQ ID NO: 748)

5'-GAAGCGCACGCUGCGGAGGCUGCUG-3' (SEQ ID NO: 1105)
3'-GCCUUCGCGUGCGACGCCUCCGACGAC-5' (SEQ ID NO: 393)
EGFR-2295 Target: 5'-CGGAAGCGCACGCTGCGGAGGCTGCTG-3' (SEQ ID NO: 749)

5'-GCGCACGCUGCGGAGGCUGCUGCAG-3' (SEQ ID NO: 1106)
3'-UUCGCGUGCGACGCCUCCGACGACGUC-5' (SEQ ID NO: 394)
EGFR-2298 Target: 5'-AAGCGCACGCTGCGGAGGCTGCTGCAG-3' (SEQ ID NO: 750)

5'-CUGAAUUCAAAAAGAUCAAAGUGCU-3' (SEQ ID NO: 1107)
3'-UUGACUUAAGUUUUUCUAGUUUCACGA-5' (SEQ ID NO: 395)
EGFR-2399 Target: 5'-AACTGAATTCAAAAAGATCAAAGTGCT-3' (SEQ ID NO: 751)

5'-AAGUGCUGGGCUCCGGUGCGUUCGG-3' (SEQ ID NO: 1108)
3'-GUUUCACGACCCGAGGCCACGCAAGCC-5' (SEQ ID NO: 396)
EGFR-2417 Target: 5'-CAAAGTGCTGGGCTCCGGTGCGTTCGG-3' (SEQ ID NO: 752)

5'-GUGCUGGGCUCCGGUGCGUUCGGCA-3' (SEQ ID NO: 1109)
3'-UUCACGACCCGAGGCCACGCAAGCCGU-5' (SEQ ID NO: 397)
EGFR-2419 Target: 5'-AAGTGCTGGGCTCCGGTGCGTTCGGCA-3' (SEQ ID NO: 753)

5'-UGCUGGGCUCCGGUGCGUUCGGCAC-3' (SEQ ID NO: 1110)
3'-UCACGACCCGAGGCCACGCAAGCCGUG-5' (SEQ ID NO: 398)
EGFR-2420 Target: 5'-AGTGCTGGGCTCCGGTGCGTTCGGCAC-3' (SEQ ID NO: 754)

5'-GCUGGGCUCCGGUGCGUUCGGCACG-3' (SEQ ID NO: 1111)
3'-CACGACCCGAGGCCACGCAAGCCGUGC-5' (SEQ ID NO: 399)
EGFR-2421 Target: 5'-GTGCTGGGCTCCGGTGCGTTCGGCACG-3' (SEQ ID NO: 755)

5'-CUGGGCUCCGGUGCGUUCGGCACGG-3' (SEQ ID NO: 1112)
3'-ACGACCCGAGGCCACGCAAGCCGUGCC-5' (SEQ ID NO: 400)
EGFR-2422 Target: 5'-TGCTGGGCTCCGGTGC GTTCGGCACGG-3' (SEQ ID NO: 756)

5'-UGUGCCGCCUGCUGGGCAUCUGCCU-3' (SEQ ID NO: 1113)
3'-GCACACGGCGGACGACCCGUAGACGGA-5' (SEQ ID NO: 401)
EGFR-2591 Target: 5'-CGTGTGCCGCTGCTGGGCATCTGCCT-3' (SEQ ID NO: 757)

5'-GUGCCGCCUGCUGGGCAUCUGCCUC-3' (SEQ ID NO: 1114)
3'-CACACGGCGGACGACCCGUAGACGGAG-5' (SEQ ID NO: 402)
EGFR-2592 Target: 5'-GTGTGCCGCTGCTGGGCATCTGCCTC-3' (SEQ ID NO: 758)

5'-GCCGCCUGCUGGGCAUCUGCCUCAC-3' (SEQ ID NO: 1115)
3'-CACGGCGGACGACCCGUAGACGGAGUG-5' (SEQ ID NO: 403)
EGFR-2594 Target: 5'-GTGCCGCTGCTGGGCATCTGCCTCAC-3' (SEQ ID NO: 759)

5'-CCGUGCAGCUCAUCACGCAGCUCAU-3' (SEQ ID NO: 1116)
3'-GUGGCACGUCGAGUAGUGCGUCGAGUA-5' (SEQ ID NO: 404)
EGFR-2624 Target: 5'-CACCGTGCAGCTCATCACGCAGCTCAT-3' (SEQ ID NO: 760)

5'-UGCAGCUCAUCACGCAGCUCAUGCC-3' (SEQ ID NO: 1117)
3'-GCACGUCGAGUAGUGCGUCGAGUACGG-5' (SEQ ID NO: 405)
EGFR-2627 Target: 5'-CGTGCAGCTCATCACGCAGCTCATGCC-3' (SEQ ID NO: 761)

5'-GCUCAUCACGCAGCUCAUGCCCUUC-3' (SEQ ID NO: 1118)
3'-GUCGAGUAGUGCGUCGAGUACGGGAAG-5' (SEQ ID NO: 406)
EGFR-2631 Target: 5'-CAGCTCATCACGCAGCTCATGCCCTTC-3' (SEQ ID NO: 762)

5'-CUCAUCACGCAGCUCAUGCCCUUCG-3' (SEQ ID NO: 1119)
3'-UCGAGUAGUGCGUCGAGUACGGGAAGC-5' (SEQ ID NO: 407)
EGFR-2632 Target: 5'-AGCTCATCACGCAGCTCATGCCCTTCG-3' (SEQ ID NO: 763)

5'-GCUCAUGCCCUUCGGCUGCCUCCUG-3' (SEQ ID NO: 1120)
3'-GUCGAGUACGGGAAGCCGACGGAGGAC-5' (SEQ ID NO: 408)
EGFR-2643 Target: 5'-CAGCTCATGCCCTTCGGCTGCCTCCTG-3' (SEQ ID NO: 764)

5'-CUCAUGCCCUUCGGCUGCCUCCUGG-3' (SEQ ID NO: 1121)
3'-UCGAGUACGGGAAGCCGACGGAGGACC-5' (SEQ ID NO: 409)
EGFR-2644 Target: 5'-AGCTCATGCCCTTCGGCTGCCTCCTGG-3' (SEQ ID NO: 765)

5'-GGAGGACCGUCGCUUGGUGCACCGC-3' (SEQ ID NO: 1122)
3'-AACCUCUGGCAGCGAACCACGUGGCG-5' (SEQ ID NO: 410)
EGFR-2754 Target: 5'-TTGGAGGACCGTCGCTTGGTGCACCGC-3' (SEQ ID NO: 766)

5'-AGGACCGUCGCUUGGUGCACCGCGA-3' (SEQ ID NO: 1123)
3'-CCUCCUGGCAGCGAACCACGUGGCGCU-5' (SEQ ID NO: 411)

EGFR-2756 Target: 5'-GGAGGACCGTCGCTTGGTGCACCGCGA-3' (SEQ ID NO: 767)

5'-GGACCGUCGCUUGGUGCACCGCGAC-3' (SEQ ID NO: 1124)

3'-CUCCUGGCAGCGAACCACGUGGCGCUG-5' (SEQ ID NO: 412)

EGFR-2757 Target: 5'-GAGGACCGTCGCTTGGTGCACCGCGAC-3' (SEQ ID NO: 768)

5'-GACCGUCGCUUGGUGCACCGCGACC-3' (SEQ ID NO: 1125)

3'-UCCUGGCAGCGAACCACGUGGCGCUGG-5' (SEQ ID NO: 413)

EGFR-2758 Target: 5'-AGGACCGTCGCTTGGTGCACCGCGACC-3' (SEQ ID NO: 769)

5'-CCGUCGCUUGGUGCACCGCGACCUG-3' (SEQ ID NO: 1126)

3'-CUGGCAGCGAACCACGUGGCGCUGGAC-5' (SEQ ID NO: 414)

EGFR-2760 Target: 5'-GACCGTCGCTTGGTGCACCGCGACCTG-3' (SEQ ID NO: 770)

5'-GUCGCUUGGUGCACCGCGACCUGGC-3' (SEQ ID NO: 1127)

3'-GGCAGCGAACCACGUGGCGCUGGACCG-5' (SEQ ID NO: 415)

EGFR-2762 Target: 5'-CCGTCGCTTGGTGCACCGCGACCTGGC-3' (SEQ ID NO: 771)

5'-CGCUUGGUGCACCGCGACCUGGCAG-3' (SEQ ID NO: 1128)

3'-CAGCGAACCACGUGGCGCUGGACCGUC-5' (SEQ ID NO: 416)

EGFR-2764 Target: 5'-GTCGCTTGGTGCACCGCGACCTGGCAG-3' (SEQ ID NO: 772)

5'-GCUUGGUGCACCGCGACCUGGCAGC-3' (SEQ ID NO: 1129)

3'-AGCGAACCACGUGGCGCUGGACCGUCG-5' (SEQ ID NO: 417)

EGFR-2765 Target: 5'-TCGCTTGGTGCACCGCGACCTGGCAGC-3' (SEQ ID NO: 773)

5'-UUGGUGCACCGCGACCUGGCAGCCA-3' (SEQ ID NO: 1130)

3'-CGAACCACGUGGCGCUGGACCGUCGGU-5' (SEQ ID NO: 418)

EGFR-2767 Target: 5'-GCTTGGTGCACCGCGACCTGGCAGCCA-3' (SEQ ID NO: 774)

5'-CAUUGGAAUCAAUUUUACACAGAAU-3' (SEQ ID NO: 1131)

3'-CCGUAACCUUAGUUAAAAUGUGUCUUA-5' (SEQ ID NO: 419)

EGFR-2915 Target: 5'-GGCATTGGAATCAATTTTACACAGAAT-3' (SEQ ID NO: 775)

5'-AAGUGCUGGAUGAUAGACGCAGAU-3' (SEQ ID NO: 1132)

3'-AGUUCACGACCUACUAUCUGCGUCUAU-5' (SEQ ID NO: 420)

EGFR-3115 Target: 5'-TCAAGTGCTGGATGATAGACGCAGATA-3' (SEQ ID NO: 776)

5'-GUGCUGGAUGAUAGACGCAGAUAGU-3' (SEQ ID NO: 1133)

3'-UUCACGACCUACUAUCUGCGUCUAUCA-5' (SEQ ID NO: 421)

EGFR-3117 Target: 5'-AAGTGCTGGATGATAGACGCAGATAGT-3' (SEQ ID NO: 777)

5'-UGCUGGAUGAUAGACGCAGAUAGUC-3' (SEQ ID NO: 1134)

3'-UCACGACCUACUAUCUGCGUCUAUCAG-5' (SEQ ID NO: 422)

EGFR-3118 Target: 5'-AGTGCTGGATGATAGACGCAGATAGTC-3' (SEQ ID NO: 778)

5'-CUGGAUGAUAGACGCAGAUAGUCGC-3' (SEQ ID NO: 1135)

3'-ACGACCUACUAUCUGCGUCUAUCAGCG-5' (SEQ ID NO: 423)
EGFR-3120 Target: 5'-TGCTGGATGATAGACGCAGATAGTCGC-3' (SEQ ID NO: 779)

5'-CCUGAGCUCUCUGAGUGCAACCAGC-3' (SEQ ID NO: 1136)
3'-GAGGACUCGAGAGACUCACGUUGGUCG-5' (SEQ ID NO: 424)
EGFR-3372 Target: 5'-CTCCTGAGCTCTCTGAGTGCAACCAGC-3' (SEQ ID NO: 780)

5'-GAGCUCUCUGAGUGCAACCAGCAAC-3' (SEQ ID NO: 1137)
3'-GACUCGAGAGACUCACGUUGGUCGUUG-5' (SEQ ID NO: 425)
EGFR-3375 Target: 5'-CTGAGCTCTCTGAGTGCAACCAGCAAC-3' (SEQ ID NO: 781)

5'-GCUGUCCCAUCAAGGAAGACAGCUU-3' (SEQ ID NO: 1138)
3'-UUCGACAGGGUAGUUCUUCUGUCGAA-5' (SEQ ID NO: 426)
EGFR-3440 Target: 5'-AAGCTGTCCCATCAAGGAAGACAGCTT-3' (SEQ ID NO: 782)

5'-CUGUCCCAUCAAGGAAGACAGCUUC-3' (SEQ ID NO: 1139)
3'-UCGACAGGGUAGUUCUUCUGUCGAAG-5' (SEQ ID NO: 427)
EGFR-3441 Target: 5'-AGCTGTCCCATCAAGGAAGACAGCTTC-3' (SEQ ID NO: 783)

5'-GACAGCUUCUUGCAGCGAUACAGCU-3' (SEQ ID NO: 1140)
3'-UUCUGUCGAAGAACGUCGCUAUGUCGA-5' (SEQ ID NO: 428)
EGFR-3457 Target: 5'-AAGACAGCTTCTTGACGCGATACAGCT-3' (SEQ ID NO: 784)

5'-ACAGCUUCUUGCAGCGAUACAGCUC-3' (SEQ ID NO: 1141)
3'-UCUGUCGAAGAACGUCGCUAUGUCGAG-5' (SEQ ID NO: 429)
EGFR-3458 Target: 5'-AGACAGCTTCTTGACGCGATACAGCTC-3' (SEQ ID NO: 785)

5'-CAGCUUCUUGCAGCGAUACAGCUCA-3' (SEQ ID NO: 1142)
3'-CUGUCGAAGAACGUCGCUAUGUCGAGU-5' (SEQ ID NO: 430)
EGFR-3459 Target: 5'-GACAGCTTCTTGACGCGATACAGCTCA-3' (SEQ ID NO: 786)

5'-AGCUUCUUGCAGCGAUACAGCUCAG-3' (SEQ ID NO: 1143)
3'-UGUCGAAGAACGUCGCUAUGUCGAGUC-5' (SEQ ID NO: 431)
EGFR-3460 Target: 5'-ACAGCTTCTTGACGCGATACAGCTCAG-3' (SEQ ID NO: 787)

5'-GCUUCUUGCAGCGAUACAGCUCAGA-3' (SEQ ID NO: 1144)
3'-GUCGAAGAACGUCGCUAUGUCGAGUCU-5' (SEQ ID NO: 432)
EGFR-3461 Target: 5'-CAGCTTCTTGACGCGATACAGCTCAGA-3' (SEQ ID NO: 788)

5'-UUCUUGCAGCGAUACAGCUCAGACC-3' (SEQ ID NO: 1145)
3'-CGAAGAACGUCGCUAUGUCGAGUCUGG-5' (SEQ ID NO: 433)
EGFR-3463 Target: 5'-GCTTCTTGACGCGATACAGCTCAGACC-3' (SEQ ID NO: 789)

5'-ACAAAGCAGUGAAUUUAUUGGAGCA-3' (SEQ ID NO: 1146)
3'-GGUGUUUCGUCACUAAUAACCUCGU-5' (SEQ ID NO: 434)
EGFR-3876 Target: 5'-CCACAAAGCAGTGAATTTATTGGAGCA-3' (SEQ ID NO: 790)

5'-AUUUUUGAAAAAAAAAAAAAGUAUA-3' (SEQ ID NO: 1147)
3'-CAUAUAAACUUUUUUUUUUUCAUAU-5' (SEQ ID NO: 435)
EGFR-4178 Target: 5'-GTATATTTGAAAAAAAAAAAAAGTATA-3' (SEQ ID NO: 791)

5'-UGAGGAUUUUUAUUGAUUGGGGAUC-3' (SEQ ID NO: 1148)
3'-ACACUCCUAAAAAUAACUAACCCCUAG-5' (SEQ ID NO: 436)
EGFR-4205 Target: 5'-TGTGAGGATTTTTATTGATTGGGGATC-3' (SEQ ID NO: 792)

5'-CUAUUGAUUUUUACUUCAAUGGGCU-3' (SEQ ID NO: 1149)
3'-GCGAUAACUAAAAUGAAGUUACCCGA-5' (SEQ ID NO: 437)
EGFR-4249 Target: 5'-CGCTATTGATTTTTACTTCAATGGGCT-3' (SEQ ID NO: 793)

5'-GGAAGAAGCUUGCUGGUAGCACUUG-3' (SEQ ID NO: 1150)
3'-UCCUUCUUCGAACGACCAUCGUGAAC-5' (SEQ ID NO: 438)
EGFR-4284 Target: 5'-AAGGAAGAAGCTTGCTGGTAGCACTTG-3' (SEQ ID NO: 794)

5'-GAAGAAGCUUGCUGGUAGCACUUGC-3' (SEQ ID NO: 1151)
3'-UCCUUCUUCGAACGACCAUCGUGAACG-5' (SEQ ID NO: 439)
EGFR-4285 Target: 5'-AGGAAGAAGCTTGCTGGTAGCACTTGC-3' (SEQ ID NO: 795)

5'-AAGAAGCUUGCUGGUAGCACUUGCU-3' (SEQ ID NO: 1152)
3'-CCUUCUUCGAACGACCAUCGUGAACGA-5' (SEQ ID NO: 440)
EGFR-4286 Target: 5'-GGAAGAAGCTTGCTGGTAGCACTTGCT-3' (SEQ ID NO: 796)

5'-AGAAGCUUGCUGGUAGCACUUGCUA-3' (SEQ ID NO: 1153)
3'-CUUCUUCGAACGACCAUCGUGAACGAU-5' (SEQ ID NO: 441)
EGFR-4287 Target: 5'-GAAGAAGCTTGCTGGTAGCACTTGCTA-3' (SEQ ID NO: 797)

5'-GAAGCUUGCUGGUAGCACUUGCUAC-3' (SEQ ID NO: 1154)
3'-UUCUUCGAACGACCAUCGUGAACGAUG-5' (SEQ ID NO: 442)
EGFR-4288 Target: 5'-AAGAAGCTTGCTGGTAGCACTTGCTAC-3' (SEQ ID NO: 798)

5'-AGCUUGCUGGUAGCACUUGCUACCC-3' (SEQ ID NO: 1155)
3'-CUUCGAACGACCAUCGUGAACGAUGGG-5' (SEQ ID NO: 443)
EGFR-4290 Target: 5'-GAAGCTTGCTGGTAGCACTTGCTACCC-3' (SEQ ID NO: 799)

5'-GCUUGCUGGUAGCACUUGCUACCCU-3' (SEQ ID NO: 1156)
3'-UUCGAACGACCAUCGUGAACGAUGGGA-5' (SEQ ID NO: 444)
EGFR-4291 Target: 5'-AAGCTTGCTGGTAGCACTTGCTACCCT-3' (SEQ ID NO: 800)

5'-CUUGCUGGUAGCACUUGCUACCCUG-3' (SEQ ID NO: 1157)
3'-UCGAACGACCAUCGUGAACGAUGGGAC-5' (SEQ ID NO: 445)
EGFR-4292 Target: 5'-AGCTTGCTGGTAGCACTTGCTACCCTG-3' (SEQ ID NO: 801)

5'-UUGCUGGUAGCACUUGCUACCCUGA-3' (SEQ ID NO: 1158)
3'-CGAACGACCAUCGUGAACGAUGGGACU-5' (SEQ ID NO: 446)
EGFR-4293 Target: 5'-GCTTGCTGGTAGCACTTGCTACCCTGA-3' (SEQ ID NO: 802)

5'-UGCUGGUAGCACUUGCUACCCUGAG-3' (SEQ ID NO: 1159)
3'-GAACGACCAUCGUGAACGAUGGGACUC-5' (SEQ ID NO: 447)
EGFR-4294 Target: 5'-CTTGCTGGTAGCACTTGCTACCCTGAG-3' (SEQ ID NO: 803)

5'-GCUGGUAGCACUUGCUACCCUGAGU-3' (SEQ ID NO: 1160)
3'-AACGACCAUCGUGAACGAUGGGACUCA-5' (SEQ ID NO: 448)
EGFR-4295 Target: 5'-TTGCTGGTAGCACTTGCTACCCTGAGT-3' (SEQ ID NO: 804)

5'-AUGCUUGAUUCCAGUGGUUCUGCUU-3' (SEQ ID NO: 1161)
3'-CCUACGAACUAAGGUCACCAAGACGAA-5' (SEQ ID NO: 449)
EGFR-4372 Target: 5'-GGATGCTTGATTCCAGTGGTTCTGCTT-3' (SEQ ID NO: 805)

5'-UGCUGAUUCCAGUGGUUCUGCUUC-3' (SEQ ID NO: 1162)
3'-CUACGAACUAAGGUCACCAAGACGAAG-5' (SEQ ID NO: 450)
EGFR-4373 Target: 5'-GATGCTTGATTCCAGTGGTTCTGCTTC-3' (SEQ ID NO: 806)

5'-CAGGCCGGAUCGGUACUGUAUCAAG-3' (SEQ ID NO: 1163)
3'-UCGUCCGGCCUAGCCAUGACAUAUAGUUC-5' (SEQ ID NO: 451)
EGFR-4450 Target: 5'-AGCAGGCCGGATCGGTACTGTATCAAG-3' (SEQ ID NO: 807)

5'-CGGAUCGGUACUGUAUCAAGUCAUG-3' (SEQ ID NO: 1164)
3'-CGGCCUAGCCAUGACAUAUAGUUCAGUAC-5' (SEQ ID NO: 452)
EGFR-4455 Target: 5'-GCCGGATCGGTACTGTATCAAGTCATG-3' (SEQ ID NO: 808)

5'-CUUAGACUUACUUUUUGUAAAAAUGU-3' (SEQ ID NO: 1165)
3'-AGGAAUCUGAAUGAAAACAUUUUUACA-5' (SEQ ID NO: 453)
EGFR-4550 Target: 5'-TCCTTAGACTTACTTTTGTA AAAATGT-3' (SEQ ID NO: 809)

5'-GUCUUGCUGUCAUGAAAUCAGCAAG-3' (SEQ ID NO: 1166)
3'-GACAGAACGACAGUACUUUAGUCGUUC-5' (SEQ ID NO: 454)
EGFR-4684 Target: 5'-CTGTCTTGCTGTCATGAAATCAGCAAG-3' (SEQ ID NO: 810)

5'-UAAGGAUAGCACCGCUUUUGUUCUC-3' (SEQ ID NO: 1167)
3'-GGAUUCUAUCGUGGCGAAAACAAGAG-5' (SEQ ID NO: 455)
EGFR-4804 Target: 5'-CCTAAGGATAGCACCGCTTTTGTTCTC-3' (SEQ ID NO: 811)

5'-AGGAUAGCACCGCUUUUGUUCUCGC-3' (SEQ ID NO: 1168)
3'-AUUCCUAUCGUGGCGAAAACAAGAGCG-5' (SEQ ID NO: 456)
EGFR-4806 Target: 5'-TAAGGATAGCACCGCTTTTGTTCTCGC-3' (SEQ ID NO: 812)

5'-GGAUAGCACCGCUUUUGUUCUCGCA-3' (SEQ ID NO: 1169)
3'-UUCUAUCGUGGCGAAAACAAGAGCGU-5' (SEQ ID NO: 457)
EGFR-4807 Target: 5'-AAGGATAGCACCGCTTTTGTTCTCGCA-3' (SEQ ID NO: 813)

5'-GAUAGCACCGCUUUUGUUCUCGCAA-3' (SEQ ID NO: 1170)
3'-UCCUAUCGUGGCGAAAACAAGAGCGUU-5' (SEQ ID NO: 458)

EGFR-4808 Target: 5'-AGGATAGCACCGCTTTTGTTCCTCGCAA-3' (SEQ ID NO: 814)

5'-AUAGCACCGCUUUUGUUCUCGCAAA-3' (SEQ ID NO: 1171)

3'-CCUAUCGUGGCGAAAACAAGAGCGUUU-5' (SEQ ID NO: 459)

EGFR-4809 Target: 5'-GGATAGCACCGCTTTTGTTCCTCGCAA-3' (SEQ ID NO: 815)

5'-UAGCACCGCUUUUGUUCUCGCAAAA-3' (SEQ ID NO: 1172)

3'-CUAUCGUGGCGAAAACAAGAGCGUUU-5' (SEQ ID NO: 460)

EGFR-4810 Target: 5'-GATAGCACCGCTTTTGTTCCTCGCAAAA-3' (SEQ ID NO: 816)

5'-AGCACCGCUUUUGUUCUCGCAAAAA-3' (SEQ ID NO: 1173)

3'-UAUCGUGGCGAAAACAAGAGCGUUUU-5' (SEQ ID NO: 461)

EGFR-4811 Target: 5'-ATAGCACCGCTTTTGTTCCTCGCAAAAA-3' (SEQ ID NO: 817)

5'-GCACCGCUUUUGUUCUCGCAAAAAAC-3' (SEQ ID NO: 1174)

3'-AUCGUGGCGAAAACAAGAGCGUUUUUG-5' (SEQ ID NO: 462)

EGFR-4812 Target: 5'-TAGCACCGCTTTTGTTCCTCGCAAAAAAC-3' (SEQ ID NO: 818)

5'-CACCGCUUUUGUUCUCGCAAAAAACG-3' (SEQ ID NO: 1175)

3'-UCGUGGCGAAAACAAGAGCGUUUUUGC-5' (SEQ ID NO: 463)

EGFR-4813 Target: 5'-AGCACCGCTTTTGTTCCTCGCAAAAAACG-3' (SEQ ID NO: 819)

5'-CGCUUUUGUUCUCGCAAAAAACGUAU-3' (SEQ ID NO: 1176)

3'-UGGCGAAAACAAGAGCGUUUUUGCAUA-5' (SEQ ID NO: 464)

EGFR-4816 Target: 5'-ACCGCTTTTGTTCCTCGCAAAAAACGTAT-3' (SEQ ID NO: 820)

5'-GCUUUUGUUCUCGCAAAAAACGUUUC-3' (SEQ ID NO: 1177)

3'-GGCGAAAACAAGAGCGUUUUUGCAUAG-5' (SEQ ID NO: 465)

EGFR-4817 Target: 5'-CCGCTTTTGTTCCTCGCAAAAAACGTATC-3' (SEQ ID NO: 821)

5'-CUUUUGUUCUCGCAAAAAACGUUUCU-3' (SEQ ID NO: 1178)

3'-GCGAAAACAAGAGCGUUUUUGCAUAGA-5' (SEQ ID NO: 466)

EGFR-4818 Target: 5'-CGCTTTTGTTCCTCGCAAAAAACGTATCT-3' (SEQ ID NO: 822)

5'-UUUUGUUCUCGCAAAAAACGUUUCUC-3' (SEQ ID NO: 1179)

3'-CGAAAACAAGAGCGUUUUUGCAUAGAG-5' (SEQ ID NO: 467)

EGFR-4819 Target: 5'-GCTTTTGTTCCTCGCAAAAAACGTATCTC-3' (SEQ ID NO: 823)

5'-UUCUCGCAAAAAACGUUUCUCCUAAU-3' (SEQ ID NO: 1180)

3'-ACAAGAGCGUUUUUGCAUAGAGGAUUA-5' (SEQ ID NO: 468)

EGFR-4824 Target: 5'-TGTTCTCGCAAAAAACGTATCTCCTAAT-3' (SEQ ID NO: 824)

5'-AAAUUAGUUUGUGUUACUUAUGGAA-3' (SEQ ID NO: 1181)

3'-GUUUUAAUCAAAACACAAUGAAUACCUU-5' (SEQ ID NO: 469)

EGFR-4953 Target: 5'-CAAAATTAGTTTGTTACTTATGGAA-3' (SEQ ID NO: 825)

5'-UUAUGGAAGAUAGUUUUCUCCUUUU-3' (SEQ ID NO: 1182)

3'-UGAAUACCUUCUAUCAAAGAGGAAAA-5' (SEQ ID NO: 470)
EGFR-4970 Target: 5'-ACTTATGGAAGATAGTTTTCTCCTTT-3' (SEQ ID NO: 826)

5'-UCAAAGCUUUUUACUCAAGAGUA-3' (SEQ ID NO: 1183)
3'-GAAGUUUUCGAAAAUGAGUUUCUCAU-5' (SEQ ID NO: 471)
EGFR-5003 Target: 5'-CTTCAAAAGCTTTTTACTCAAAGAGTA-3' (SEQ ID NO: 827)

5'-ACUAGGGUUUGAAAUUGAUAAUGCU-3' (SEQ ID NO: 1184)
3'-UUUGAUCCCAAACUUUAACUAUUACGA-5' (SEQ ID NO: 472)
EGFR-5206 Target: 5'-AAACTAGGGTTTGAAATTGATAATGCT-3' (SEQ ID NO: 828)

5'-UAAAAUAAUUCUCUACAAUUGGAA-3' (SEQ ID NO: 1185)
3'-GGAUUUUUAAAGAGAUGUUAACCUU-5' (SEQ ID NO: 473)
EGFR-5275 Target: 5'-CCTAAATAATTTCTCTACAATTGGAA-3' (SEQ ID NO: 829)

5'-CAGCAGUCCUUUGUAAACAGUGUUU-3' (SEQ ID NO: 1186)
3'-UUGUCGUCAGGAAACAUUUGUCACAAA-5' (SEQ ID NO: 474)
EGFR-5374 Target: 5'-AACAGCAGTCCTTTGTAAACAGTGTTT-3' (SEQ ID NO: 830)

5'-CAAUUUUAUCAAGGAAGAAAUGGUUC-3' (SEQ ID NO: 1187)
3'-AGGUUAAAAGUUCUUCUUUACCAAG-5' (SEQ ID NO: 475)
EGFR-5429 Target: 5'-TCCAATTTATCAAGGAAGAAATGGTTC-3' (SEQ ID NO: 831)

5'-UACAAAAUGUCCUUUUUGCUUUUAA-3' (SEQ ID NO: 1188)
3'-GUAUGUUUUACAAGGAAACGAAAAUU-5' (SEQ ID NO: 476)
EGFR-5497 Target: 5'-CATACAAAATGTTCTTTTGCTTTTAA-3' (SEQ ID NO: 832)

5'-GUUCCUUUUGCUUUUAAAGUAAUUU-3' (SEQ ID NO: 1189)
3'-UACAAGGAAACGAAAAUUUCAUAAAA-5' (SEQ ID NO: 477)
EGFR-5505 Target: 5'-ATGTTCTTTTGCTTTTAAAGTAATTT-3' (SEQ ID NO: 833)

5'-UUCCUUUUGCUUUUAAAGUAAUUUU-3' (SEQ ID NO: 1190)
3'-ACAAGGAAACGAAAAUUUCAUAAAA-5' (SEQ ID NO: 478)
EGFR-5506 Target: 5'-TGTTCTTTTGCTTTTAAAGTAATTTT-3' (SEQ ID NO: 834)

5'-UUGCUUUUAAAGUAAUUUUUGACUC-3' (SEQ ID NO: 1191)
3'-AAAACGAAAAUUUCAUAAAAACUGAG-5' (SEQ ID NO: 479)
EGFR-5512 Target: 5'-TTTTGCTTTTAAAGTAATTTTGACTC-3' (SEQ ID NO: 835)

5'-GUUAAGAAAGUAUUUGAUUUUUGUC-3' (SEQ ID NO: 1192)
3'-AACAAUUCUUUCAUAAACUAAAAACAG-5' (SEQ ID NO: 480)
EGFR-5565 Target: 5'-TTGTTAAGAAAGTATTTGATTTTGTGTC-3' (SEQ ID NO: 836)

5'-UUGGAAAUUACCUAUGUGCAGAGGA-3' (SEQ ID NO: 1193)
3'-UAAACCUUAAUGGAUACACGUCUCCU-5' (SEQ ID NO: 481)
EGFR-463 Target: 5'-ATTTGGAAATTACCTATGTGCAGAGGA-3' (SEQ ID NO: 837)

5'-UGGAAAUUACCUAUGUGCAGAGGAA-3' (SEQ ID NO: 1194)
3'-AAACCUUUAAUGGAUACACGUCUCCUU-5' (SEQ ID NO: 482)

EGFR-464 Target: 5'-TTTGAAATTACCTATGTGCAGAGGAA-3' (SEQ ID NO: 838)

5'-CUUUCUUCUUAAGACCAUCCAGG-3' (SEQ ID NO: 1195)
3'-UAGAAAGGAAGAAUUUCUGGUAGGUCC-5' (SEQ ID NO: 483)

EGFR-496 Target: 5'-ATCTTTCCTTCTTAAAGACCATCCAGG-3' (SEQ ID NO: 839)

5'-UUUCCUUCUUAAGACCAUCCAGGA-3' (SEQ ID NO: 1196)
3'-AGAAAGGAAGAAUUUCUGGUAGGUCCU-5' (SEQ ID NO: 484)

EGFR-497 Target: 5'-TCTTTCCTTCTTAAAGACCATCCAGGA-3' (SEQ ID NO: 840)

5'-UUCUUCUUAAGACCAUCCAGGAG-3' (SEQ ID NO: 1197)
3'-GAAAGGAAGAAUUUCUGGUAGGUCCUC-5' (SEQ ID NO: 485)

EGFR-498 Target: 5'-CTTTCCTTCTTAAAGACCATCCAGGAG-3' (SEQ ID NO: 841)

5'-UCCUUCUUAAGACCAUCCAGGAGG-3' (SEQ ID NO: 1198)
3'-AAAGGAAGAAUUUCUGGUAGGUCCUCC-5' (SEQ ID NO: 486)

EGFR-499 Target: 5'-TTTCCTTCTTAAAGACCATCCAGGAGG-3' (SEQ ID NO: 842)

5'-CCUUCUUAAGACCAUCCAGGAGGU-3' (SEQ ID NO: 1199)
3'-AAGGAAGAAUUUCUGGUAGGUCCUCCA-5' (SEQ ID NO: 487)

EGFR-500 Target: 5'-TTCCTTCTTAAAGACCATCCAGGAGGT-3' (SEQ ID NO: 843)

5'-CUUCUUAAGACCAUCCAGGAGGUG-3' (SEQ ID NO: 1200)
3'-AGGAAGAAUUUCUGGUAGGUCCUCCAC-5' (SEQ ID NO: 488)

EGFR-501 Target: 5'-TCCTTCTTAAAGACCATCCAGGAGGTG-3' (SEQ ID NO: 844)

5'-UUCUUAAGACCAUCCAGGAGGUGG-3' (SEQ ID NO: 1201)
3'-GGAAGAAUUUCUGGUAGGUCCUCCACC-5' (SEQ ID NO: 489)

EGFR-502 Target: 5'-CCTTCTTAAAGACCATCCAGGAGGTGG-3' (SEQ ID NO: 845)

5'-UCUUAAGACCAUCCAGGAGGUGGC-3' (SEQ ID NO: 1202)
3'-GAAGAAUUUCUGGUAGGUCCUCCACCG-5' (SEQ ID NO: 490)

EGFR-503 Target: 5'-CTTCTTAAAGACCATCCAGGAGGTGGC-3' (SEQ ID NO: 846)

5'-CUUAAGACCAUCCAGGAGGUGGCU-3' (SEQ ID NO: 1203)
3'-AAGAAUUUCUGGUAGGUCCUCCACCGA-5' (SEQ ID NO: 491)

EGFR-504 Target: 5'-TTCTTAAAGACCATCCAGGAGGTGGCT-3' (SEQ ID NO: 847)

5'-UUAAGACCAUCCAGGAGGUGGCUG-3' (SEQ ID NO: 1204)
3'-AGAAUUUCUGGUAGGUCCUCCACCGAC-5' (SEQ ID NO: 492)

EGFR-505 Target: 5'-TCTTAAAGACCATCCAGGAGGTGGCTG-3' (SEQ ID NO: 848)

5'-UAAAGACCAUCCAGGAGGUGGCUGG-3' (SEQ ID NO: 1205)
3'-GAAUUUCUGGUAGGUCCUCCACCGACC-5' (SEQ ID NO: 493)

EGFR-506 Target: 5'-CTTAAAGACCATCCAGGAGGTGGCTGG-3' (SEQ ID NO: 849)

5'-AAAGACCAUCCAGGAGGUGGCUGGU-3' (SEQ ID NO: 1206)
3'-AAUUUCUGGUAGGUCCUCCACCGACCA-5' (SEQ ID NO: 494)

EGFR-507 Target: 5'-TTAAAGACCATCCAGGAGGTGGCTGGT-3' (SEQ ID NO: 850)

5'-AAGACCAUCCAGGAGGUGGCUGGU-3' (SEQ ID NO: 1207)
3'-AUUUCUGGUAGGUCCUCCACCGACCAA-5' (SEQ ID NO: 495)

EGFR-508 Target: 5'-TAAAGACCATCCAGGAGGTGGCTGGTT-3' (SEQ ID NO: 851)

5'-AGACCAUCCAGGAGGUGGCUGGUUA-3' (SEQ ID NO: 1208)
3'-UUUCUGGUAGGUCCUCCACCGACCAAU-5' (SEQ ID NO: 496)

EGFR-509 Target: 5'-AAAGACCATCCAGGAGGTGGCTGGTTA-3' (SEQ ID NO: 852)

5'-UGUGAUCCAAGCUGUCCCAAUGGGA-3' (SEQ ID NO: 1209)
3'-UCACACUAGGUUCGACAGGGUUACCCU-5' (SEQ ID NO: 497)

EGFR-838 Target: 5'-AGTGTGATCCAAGCTGTCCCAATGGGA-3' (SEQ ID NO: 853)

5'-GUGAUCCAAGCUGUCCCAAUGGGAG-3' (SEQ ID NO: 1210)
3'-CACACUAGGUUCGACAGGGUUACCCUC-5' (SEQ ID NO: 498)

EGFR-839 Target: 5'-GTGTGATCCAAGCTGTCCCAATGGGAG-3' (SEQ ID NO: 854)

5'-UGAUCCAAGCUGUCCCAAUGGGAGC-3' (SEQ ID NO: 1211)
3'-ACACUAGGUUCGACAGGGUUACCCUCG-5' (SEQ ID NO: 499)

EGFR-840 Target: 5'-TGTGATCCAAGCTGTCCCAATGGGAGC-3' (SEQ ID NO: 855)

5'-GAUCCAAGCUGUCCCAAUGGGAGCU-3' (SEQ ID NO: 1212)
3'-CACUAGGUUCGACAGGGUUACCCUCGA-5' (SEQ ID NO: 500)

EGFR-841 Target: 5'-GTGATCCAAGCTGTCCCAATGGGAGCT-3' (SEQ ID NO: 856)

5'-AUCCAAGCUGUCCCAAUGGGAGCUG-3' (SEQ ID NO: 1213)
3'-ACUAGGUUCGACAGGGUUACCCUCGAC-5' (SEQ ID NO: 501)

EGFR-842 Target: 5'-TGATCCAAGCTGTCCCAATGGGAGCTG-3' (SEQ ID NO: 857)

5'-AGGAGAGGAGAACUGCCAGAAACUG-3' (SEQ ID NO: 1214)
3'-CGUCCUCUCCUCUUGACGGUCUUUGAC-5' (SEQ ID NO: 502)

EGFR-876 Target: 5'-GCAGGAGAGGAGAACTGCCAGAAACTG-3' (SEQ ID NO: 858)

5'-GGAGAGGAGAACUGCCAGAAACUGA-3' (SEQ ID NO: 1215)
3'-GUCCUCUCCUCUUGACGGUCUUUGACU-5' (SEQ ID NO: 503)

EGFR-877 Target: 5'-CAGGAGAGGAGAACTGCCAGAAACTGA-3' (SEQ ID NO: 859)

5'-GAGAGGAGAACUGCCAGAAACUGAC-3' (SEQ ID NO: 1216)
3'-UCCUCUCCUCUUGACGGUCUUUGACUG-5' (SEQ ID NO: 504)

EGFR-878 Target: 5'-AGGAGAGGAGAACTGCCAGAAACTGAC-3' (SEQ ID NO: 860)

5'-AGAGGAGAACUGCCAGAAACUGACC-3' (SEQ ID NO: 1217)
3'-CCUCUCCUCUUGACGGUCUUUGACUGG-5' (SEQ ID NO: 505)

EGFR-879 Target: 5'-GGAGAGGAGAACTGCCAGAACTGACC-3' (SEQ ID NO: 861)

5'-UGACCAAAAUCAUCUGUGCCCAGCA-3' (SEQ ID NO: 1218)
3'-UGACUGGUUUUAGUAGACACGGGUCGU-5' (SEQ ID NO: 506)

EGFR-899 Target: 5'-ACTGACCAAAATCATCTGTGCCCAGCA-3' (SEQ ID NO: 862)

5'-GACCAAAAUCAUCUGUGCCCAGCAG-3' (SEQ ID NO: 1219)
3'-GACUGGUUUUAGUAGACACGGGUCGUC-5' (SEQ ID NO: 507)

EGFR-900 Target: 5'-CTGACCAAAATCATCTGTGCCCAGCAG-3' (SEQ ID NO: 863)

5'-ACCAAAAUCAUCUGUGCCCAGCAGU-3' (SEQ ID NO: 1220)
3'-ACUGGUUUUAGUAGACACGGGUCGUCA-5' (SEQ ID NO: 508)

EGFR-901 Target: 5'-TGACCAAAATCATCTGTGCCCAGCAGT-3' (SEQ ID NO: 864)

5'-CCAAAUCAUCUGUGCCCAGCAGUG-3' (SEQ ID NO: 1221)
3'-CUGGUUUUAGUAGACACGGGUCGUCAC-5' (SEQ ID NO: 509)

EGFR-902 Target: 5'-GACCAAAATCATCTGTGCCCAGCAGTG-3' (SEQ ID NO: 865)

5'-CAAAAUCAUCUGUGCCCAGCAGUGC-3' (SEQ ID NO: 1222)
3'-UGGUUUUAGUAGACACGGGUCGUCACG-5' (SEQ ID NO: 510)

EGFR-903 Target: 5'-ACCAAAATCATCTGTGCCCAGCAGTGC-3' (SEQ ID NO: 866)

5'-AAAAUCAUCUGUGCCCAGCAGUGCU-3' (SEQ ID NO: 1223)
3'-GGUUUUAGUAGACACGGGUCGUCACGA-5' (SEQ ID NO: 511)

EGFR-904 Target: 5'-CCAAAATCATCTGTGCCCAGCAGTGCT-3' (SEQ ID NO: 867)

5'-AAAUCAUCUGUGCCCAGCAGUGCUC-3' (SEQ ID NO: 1224)
3'-GUUUUAGUAGACACGGGUCGUCACGAG-5' (SEQ ID NO: 512)

EGFR-905 Target: 5'-CAAAATCATCTGTGCCCAGCAGTGCTC-3' (SEQ ID NO: 868)

5'-CAGUGACUGCUGCCACAACCAGUGU-3' (SEQ ID NO: 1225)
3'-GGGUCACUGACGACGGUGUUGGUCACA-5' (SEQ ID NO: 513)

EGFR-954 Target: 5'-CCCAGTGACTGCTGCCACAACCAGTGT-3' (SEQ ID NO: 869)

5'-AGUGACUGCUGCCACAACCAGUGUG-3' (SEQ ID NO: 1226)
3'-GGUCACUGACGACGGUGUUGGUCACAC-5' (SEQ ID NO: 514)

EGFR-955 Target: 5'-CCAGTGACTGCTGCCACAACCAGTGTG-3' (SEQ ID NO: 870)

5'-GUGACUGCUGCCACAACCAGUGUGC-3' (SEQ ID NO: 1227)
3'-GUCACUGACGACGGUGUUGGUCACACG-5' (SEQ ID NO: 515)

EGFR-956 Target: 5'-CAGTGACTGCTGCCACAACCAGTGTGC-3' (SEQ ID NO: 871)

5'-CACUCUCCAUAUUUACGAUUAU-3' (SEQ ID NO: 1228)
3'-GAGUGAGAGGUUUUACGAUUAUA-5' (SEQ ID NO: 516)

EGFR-1313 Target: 5'-CTCACTCTCCATAAATGCTACGAATAT-3' (SEQ ID NO: 872)

5'-UUUUUGCUGAUUCAGGCUUGGCCUG-3' (SEQ ID NO: 1229)

3'-CCAAAAACGACUAAGUCCGAACCGGAC-5' (SEQ ID NO: 517)
EGFR-1480 Target: 5'-GGTTTTTGCTGATTCAGGCTTGGCCTG-3' (SEQ ID NO: 873)

5'-UUUUGCUGAUUCAGGCUUGGCCUGA-3' (SEQ ID NO: 1230)
3'-CAAAAACGACUAAGUCCGAACCGGACU-5' (SEQ ID NO: 518)
EGFR-1481 Target: 5'-GTTTTTGCTGATTCAGGCTTGGCCTGA-3' (SEQ ID NO: 874)

5'-UUUGCUGAUUCAGGCUUGGCCUGAA-3' (SEQ ID NO: 1231)
3'-AAAAACGACUAAGUCCGAACCGGACUU-5' (SEQ ID NO: 519)
EGFR-1482 Target: 5'-TTTTTGCTGATTCAGGCTTGGCCTGAA-3' (SEQ ID NO: 875)

5'-UUGCUGAUUCAGGCUUGGCCUGAAA-3' (SEQ ID NO: 1232)
3'-AAAACGACUAAGUCCGAACCGGACUUU-5' (SEQ ID NO: 520)
EGFR-1483 Target: 5'-TTTTGCTGATTCAGGCTTGGCCTGAAA-3' (SEQ ID NO: 876)

5'-UGCUGAUUCAGGCUUGGCCUGAAAA-3' (SEQ ID NO: 1233)
3'-AAACGACUAAGUCCGAACCGGACUUUU-5' (SEQ ID NO: 521)
EGFR-1484 Target: 5'-TTTGCTGATTCAGGCTTGGCCTGAAAA-3' (SEQ ID NO: 877)

5'-GCUGAUUCAGGCUUGGCCUGAAAAC-3' (SEQ ID NO: 1234)
3'-AACGACUAAGUCCGAACCGGACUUUUG-5' (SEQ ID NO: 522)
EGFR-1485 Target: 5'-TTGCTGATTCAGGCTTGGCCTGAAAAC-3' (SEQ ID NO: 878)

5'-CUGAUUCAGGCUUGGCCUGAAAACA-3' (SEQ ID NO: 1235)
3'-ACGACUAAGUCCGAACCGGACUUUUGU-5' (SEQ ID NO: 523)
EGFR-1486 Target: 5'-TGCTGATTCAGGCTTGGCCTGAAAACA-3' (SEQ ID NO: 879)

5'-UGAUUCAGGCUUGGCCUGAAAACAG-3' (SEQ ID NO: 1236)
3'-CGACUAAGUCCGAACCGGACUUUUGUC-5' (SEQ ID NO: 524)
EGFR-1487 Target: 5'-GCTGATTCAGGCTTGGCCTGAAAACAG-3' (SEQ ID NO: 880)

5'-AAGCAACAUGGUCAGUUUUCUCUUG-3' (SEQ ID NO: 1237)
3'-GGUUCGUUGUACCAGUCAAAAAGAGAAC-5' (SEQ ID NO: 525)
EGFR-1561 Target: 5'-CCAAGCAACATGGTCAGTTTTCTCTTG-3' (SEQ ID NO: 881)

5'-AGCAACAUGGUCAGUUUUCUCUUGC-3' (SEQ ID NO: 1238)
3'-GUUCGUUGUACCAGUCAAAAAGAGAACG-5' (SEQ ID NO: 526)
EGFR-1562 Target: 5'-CAAGCAACATGGTCAGTTTTCTCTTGC-3' (SEQ ID NO: 882)

5'-GCAACAUGGUCAGUUUUCUCUUGCA-3' (SEQ ID NO: 1239)
3'-UUCGUUGUACCAGUCAAAAAGAGAACGU-5' (SEQ ID NO: 527)
EGFR-1563 Target: 5'-AAGCAACATGGTCAGTTTTCTCTTGCA-3' (SEQ ID NO: 883)

5'-CAAUAAACUGGAAAAAACUGUUUGG-3' (SEQ ID NO: 1240)
3'-AUGUUAUUUGACCUUUUUUGACAAACC-5' (SEQ ID NO: 528)
EGFR-1691 Target: 5'-TACAATAAACTGGAAAAAACTGTTTGG-3' (SEQ ID NO: 884)

5'-CAGGCCAUGAACAUACCUGCACAG-3' (SEQ ID NO: 1241)
3'-GAGUCCGGUACUUGUAGUGGACGUGUC-5' (SEQ ID NO: 529)
EGFR-1963 Target: 5'-CTCAGGCCATGAACATCACCTGCACAG-3' (SEQ ID NO: 885)

5'-AGGCCAUGAACAUACCUGCACAGG-3' (SEQ ID NO: 1242)
3'-AGUCCGGUACUUGUAGUGGACGUGUCC-5' (SEQ ID NO: 530)
EGFR-1964 Target: 5'-TCAGGCCATGAACATCACCTGCACAGG-3' (SEQ ID NO: 886)

5'-AUCCAGUGUGCCCACUACAUUGACG-3' (SEQ ID NO: 1243)
3'-CAUAGGUCACACGGGUGAUGUAACUGC-5' (SEQ ID NO: 531)
EGFR-2008 Target: 5'-GTATCCAGTGTGCCCCACTACATTGACG-3' (SEQ ID NO: 887)

5'-UCCAGUGUGCCCACUACAUUGACGG-3' (SEQ ID NO: 1244)
3'-AUAGGUCACACGGGUGAUGUAACUGCC-5' (SEQ ID NO: 532)
EGFR-2009 Target: 5'-TATCCAGTGTGCCCCACTACATTGACGG-3' (SEQ ID NO: 888)

5'-CCAGUGUGCCCACUACAUUGACGGC-3' (SEQ ID NO: 1245)
3'-UAGGUCACACGGGUGAUGUAACUGCCG-5' (SEQ ID NO: 533)
EGFR-2010 Target: 5'-ATCCAGTGTGCCCCACTACATTGACGGC-3' (SEQ ID NO: 889)

5'-CAGUGUGCCCACUACAUUGACGGCC-3' (SEQ ID NO: 1246)
3'-AGGUCACACGGGUGAUGUAACUGCCGG-5' (SEQ ID NO: 534)
EGFR-2011 Target: 5'-TCCAGTGTGCCCCACTACATTGACGGCC-3' (SEQ ID NO: 890)

5'-AGUGUGCCCACUACAUUGACGGCCC-3' (SEQ ID NO: 1247)
3'-GGUCACACGGGUGAUGUAACUGCCGGG-5' (SEQ ID NO: 535)
EGFR-2012 Target: 5'-CCAGTGTGCCCCACTACATTGACGGCCC-3' (SEQ ID NO: 891)

5'-GAAUUCAAAAAGAUCAAAGUGCUGG-3' (SEQ ID NO: 1248)
3'-GACUUAAGUUUUUCUAGUUUCACGACC-5' (SEQ ID NO: 536)
EGFR-2401 Target: 5'-CTGAATTCAAAAAGATCAAAGTGCTGG-3' (SEQ ID NO: 892)

5'-AAUUCAAAAAGAUCAAAGUGCUGGG-3' (SEQ ID NO: 1249)
3'-ACUUAAGUUUUUCUAGUUUCACGACCC-5' (SEQ ID NO: 537)
EGFR-2402 Target: 5'-TGAATTCAAAAAGATCAAAGTGCTGGG-3' (SEQ ID NO: 893)

5'-CUCUGGAUCCCAGAAGGUGAGAAAG-3' (SEQ ID NO: 1250)
3'-CUGAGACCUAGGGUCUCCACUCUUUC-5' (SEQ ID NO: 538)
EGFR-2458 Target: 5'-GACTCTGGATCCCAGAAGGTGAGAAAG-3' (SEQ ID NO: 894)

5'-UCUGGAUCCCAGAAGGUGAGAAAGU-3' (SEQ ID NO: 1251)
3'-UGAGACCUAGGGUCUCCACUCUUUCA-5' (SEQ ID NO: 539)
EGFR-2459 Target: 5'-ACTCTGGATCCCAGAAGGTGAGAAAGT-3' (SEQ ID NO: 895)

5'-CUGGAUCCCAGAAGGUGAGAAAGUU-3' (SEQ ID NO: 1252)
3'-GAGACCUAGGGUCUCCACUCUUUCA-5' (SEQ ID NO: 540)
EGFR-2460 Target: 5'-CTCTGGATCCCAGAAGGTGAGAAAGTT-3' (SEQ ID NO: 896)

5'-UGGAUCCCAGAAGGUGAGAAAGUUA-3' (SEQ ID NO: 1253)
3'-AGACCUAGGGUCUCCACUCUUUCAU-5' (SEQ ID NO: 541)
EGFR-2461 Target: 5'-TCTGGATCCCAGAAGGTGAGAAAGTTA-3' (SEQ ID NO: 897)

5'-GGAUCCCAGAAGGUGAGAAAGUUA-3' (SEQ ID NO: 1254)
3'-GACCUAGGGUCUCCACUCUUUCAU-5' (SEQ ID NO: 542)
EGFR-2462 Target: 5'-CTGGATCCCAGAAGGTGAGAAAGTTAA-3' (SEQ ID NO: 898)

5'-GAUCCCAGAAGGUGAGAAAGUUA-3' (SEQ ID NO: 1255)
3'-ACCUAGGGUCUCCACUCUUUCAU-5' (SEQ ID NO: 543)
EGFR-2463 Target: 5'-TGGATCCCAGAAGGTGAGAAAGTTAAA-3' (SEQ ID NO: 899)

5'-AUCCCAGAAGGUGAGAAAGUUA-3' (SEQ ID NO: 1256)
3'-CCUAGGGUCUCCACUCUUUCAU-5' (SEQ ID NO: 544)
EGFR-2464 Target: 5'-GGATCCCAGAAGGTGAGAAAGTTAAAA-3' (SEQ ID NO: 900)

5'-UCCCAGAAGGUGAGAAAGUUA-3' (SEQ ID NO: 1257)
3'-CUAGGGUCUCCACUCUUUCAU-5' (SEQ ID NO: 545)
EGFR-2465 Target: 5'-GATCCCAGAAGGTGAGAAAGTTAAAAT-3' (SEQ ID NO: 901)

5'-CAGCAUGUCAAGAUCACAGAUUUUG-3' (SEQ ID NO: 1258)
3'-GCGUCGUACAGUUCUAGUGUCUAAAAC-5' (SEQ ID NO: 546)
EGFR-2815 Target: 5'-CGCAGCATGTCAAGATCACAGATTTTG-3' (SEQ ID NO: 902)

5'-AGCAUGUCAAGAUCACAGAUUUUGG-3' (SEQ ID NO: 1259)
3'-CGUCGUACAGUUCUAGUGUCUAAAACC-5' (SEQ ID NO: 547)
EGFR-2816 Target: 5'-GCAGCATGTCAAGATCACAGATTTTGG-3' (SEQ ID NO: 903)

5'-GCAUGUCAAGAUCACAGAUUUUGGG-3' (SEQ ID NO: 1260)
3'-GUCGUACAGUUCUAGUGUCUAAAACCC-5' (SEQ ID NO: 548)
EGFR-2817 Target: 5'-CAGCATGTCAAGATCACAGATTTTGGG-3' (SEQ ID NO: 904)

5'-CAUGUCAAGAUCACAGAUUUUGGGC-3' (SEQ ID NO: 1261)
3'-UCGUACAGUUCUAGUGUCUAAAACCCG-5' (SEQ ID NO: 549)
EGFR-2818 Target: 5'-AGCATGTCAAGATCACAGATTTTGGGC-3' (SEQ ID NO: 905)

5'-AUGUCAAGAUCACAGAUUUUGGGCU-3' (SEQ ID NO: 1262)
3'-CGUACAGUUCUAGUGUCUAAAACCCGA-5' (SEQ ID NO: 550)
EGFR-2819 Target: 5'-GCATGTCAAGATCACAGATTTTGGGCT-3' (SEQ ID NO: 906)

5'-UGUCAAGAUCACAGAUUUUGGGCUG-3' (SEQ ID NO: 1263)
3'-GUACAGUUCUAGUGUCUAAAACCCGAC-5' (SEQ ID NO: 551)
EGFR-2820 Target: 5'-CATGTCAAGATCACAGATTTTGGGCTG-3' (SEQ ID NO: 907)

5'-GUCAAGAUCACAGAUUUUGGGCUGG-3' (SEQ ID NO: 1264)
3'-UACAGUUCUAGUGUCUAAAACCCGACC-5' (SEQ ID NO: 552)

EGFR-2821 Target: 5'-ATGTCAAGATCACAGATTTTGGGCTGG-3' (SEQ ID NO: 908)

5'-UCAAGAUCACAGAUUUUGGGCUGGC-3' (SEQ ID NO: 1265)

3'-ACAGUUCUAGUGUCUAAAACCCGACCG-5' (SEQ ID NO: 553)

EGFR-2822 Target: 5'-TGTCAAGATCACAGATTTTGGGCTGGC-3' (SEQ ID NO: 909)

5'-CAAGAUCACAGAUUUUGGGCUGGCC-3' (SEQ ID NO: 1266)

3'-CAGUUCUAGUGUCUAAAACCCGACCGG-5' (SEQ ID NO: 554)

EGFR-2823 Target: 5'-GTCAAGATCACAGATTTTGGGCTGGCC-3' (SEQ ID NO: 910)

5'-AAGAUCACAGAUUUUGGGCUGGCCA-3' (SEQ ID NO: 1267)

3'-AGUUCUAGUGUCUAAAACCCGACCGGU-5' (SEQ ID NO: 555)

EGFR-2824 Target: 5'-TCAAGATCACAGATTTTGGGCTGGCCA-3' (SEQ ID NO: 911)

5'-AGAUCACAGAUUUUGGGCUGGCCAA-3' (SEQ ID NO: 1268)

3'-GUUCUAGUGUCUAAAACCCGACCGGUU-5' (SEQ ID NO: 556)

EGFR-2825 Target: 5'-CAAGATCACAGATTTTGGGCTGGCCAA-3' (SEQ ID NO: 912)

5'-GAUCACAGAUUUUGGGCUGGCCAAA-3' (SEQ ID NO: 1269)

3'-UUCUAGUGUCUAAAACCCGACCGGUUU-5' (SEQ ID NO: 557)

EGFR-2826 Target: 5'-AAGATCACAGATTTTGGGCTGGCCAAA-3' (SEQ ID NO: 913)

5'-AUCACAGAUUUUGGGCUGGCCAAAC-3' (SEQ ID NO: 1270)

3'-UCUAGUGUCUAAAACCCGACCGGUUUG-5' (SEQ ID NO: 558)

EGFR-2827 Target: 5'-AGATCACAGATTTTGGGCTGGCCAAAC-3' (SEQ ID NO: 914)

5'-UCACAGAUUUUGGGCUGGCCAAACU-3' (SEQ ID NO: 1271)

3'-CUAGUGUCUAAAACCCGACCGGUUUGA-5' (SEQ ID NO: 559)

EGFR-2828 Target: 5'-GATCACAGATTTTGGGCTGGCCAAACT-3' (SEQ ID NO: 915)

5'-CACAGAUUUUGGGCUGGCCAAACUG-3' (SEQ ID NO: 1272)

3'-UAGUGUCUAAAACCCGACCGGUUUGAC-5' (SEQ ID NO: 560)

EGFR-2829 Target: 5'-ATCACAGATTTTGGGCTGGCCAAACTG-3' (SEQ ID NO: 916)

5'-ACAGAUUUUGGGCUGGCCAAACUGC-3' (SEQ ID NO: 1273)

3'-AGUGUCUAAAACCCGACCGGUUUGACG-5' (SEQ ID NO: 561)

EGFR-2830 Target: 5'-TCACAGATTTTGGGCTGGCCAAACTGC-3' (SEQ ID NO: 917)

5'-CAGAUUUUGGGCUGGCCAAACUGCU-3' (SEQ ID NO: 1274)

3'-GUGUCUAAAACCCGACCGGUUUGACGA-5' (SEQ ID NO: 562)

EGFR-2831 Target: 5'-CACAGATTTTGGGCTGGCCAAACTGCT-3' (SEQ ID NO: 918)

5'-AGAUUUUGGGCUGGCCAAACUGCUG-3' (SEQ ID NO: 1275)

3'-UGUCUAAAACCCGACCGGUUUGACGAC-5' (SEQ ID NO: 563)

EGFR-2832 Target: 5'-ACAGATTTTGGGCTGGCCAAACTGCTG-3' (SEQ ID NO: 919)

5'-GAUUUUGGGCUGGCCAAACUGCUGG-3' (SEQ ID NO: 1276)

3'-GUCUAAAACCCGACCGUUUGACGACC-5' (SEQ ID NO: 564)
EGFR-2833 Target: 5'-CAGATTTTGGGCTGGCCAAACTGCTGG-3' (SEQ ID NO: 920)

5'-AUUUUGGGCUGGCCAAACUGCUGGG-3' (SEQ ID NO: 1277)
3'-UCUAAAACCCGACCGUUUGACGACCC-5' (SEQ ID NO: 565)
EGFR-2834 Target: 5'-AGATTTTGGGCTGGCCAAACTGCTGGG-3' (SEQ ID NO: 921)

5'-UUUUGGGCUGGCCAAACUGCUGGGU-3' (SEQ ID NO: 1278)
3'-CUAAAACCCGACCGUUUGACGACCCA-5' (SEQ ID NO: 566)
EGFR-2835 Target: 5'-GATTTTGGGCTGGCCAAACTGCTGGGT-3' (SEQ ID NO: 922)

5'-UUUGGGCUGGCCAAACUGCUGGGUG-3' (SEQ ID NO: 1279)
3'-UAAAACCCGACCGUUUGACGACCCAC-5' (SEQ ID NO: 567)
EGFR-2836 Target: 5'-ATTTTGGGCTGGCCAAACTGCTGGGTG-3' (SEQ ID NO: 923)

5'-UUGGGCUGGCCAAACUGCUGGGUGC-3' (SEQ ID NO: 1280)
3'-AAAACCCGACCGUUUGACGACCCACG-5' (SEQ ID NO: 568)
EGFR-2837 Target: 5'-TTTGGGCTGGCCAAACTGCTGGGTGC-3' (SEQ ID NO: 924)

5'-GCAAAGUGCCUAUCAAGUGGAUGGC-3' (SEQ ID NO: 1281)
3'-UCCGUUUCACGGAUAGUUCACCUACCG-5' (SEQ ID NO: 569)
EGFR-2891 Target: 5'-AGGCAAAGTGCCTATCAAGTGGATGGC-3' (SEQ ID NO: 925)

5'-CAAAGUGCCUAUCAAGUGGAUGGCA-3' (SEQ ID NO: 1282)
3'-CCGUUUCACGGAUAGUUCACCUACCGU-5' (SEQ ID NO: 570)
EGFR-2892 Target: 5'-GGCAAAGTGCCTATCAAGTGGATGGCA-3' (SEQ ID NO: 926)

5'-AAAGUGCCUAUCAAGUGGAUGGCAU-3' (SEQ ID NO: 1283)
3'-CGUUUCACGGAUAGUUCACCUACCGUA-5' (SEQ ID NO: 571)
EGFR-2893 Target: 5'-GCAAAGTGCCTATCAAGTGGATGGCAT-3' (SEQ ID NO: 927)

5'-AAGUGCCUAUCAAGUGGAUGGCAUU-3' (SEQ ID NO: 1284)
3'-GUUUCACGGAUAGUUCACCUACCGUAA-5' (SEQ ID NO: 572)
EGFR-2894 Target: 5'-CAAAGTGCCTATCAAGTGGATGGCATT-3' (SEQ ID NO: 928)

5'-AGUGCCUAUCAAGUGGAUGGCAUUG-3' (SEQ ID NO: 1285)
3'-UUUCACGGAUAGUUCACCUACCGUAAC-5' (SEQ ID NO: 573)
EGFR-2895 Target: 5'-AAAGTGCCTATCAAGTGGATGGCATTG-3' (SEQ ID NO: 929)

5'-GUGCCUAUCAAGUGGAUGGCAUUGG-3' (SEQ ID NO: 1286)
3'-UUCACGGAUAGUUCACCUACCGUAACC-5' (SEQ ID NO: 574)
EGFR-2896 Target: 5'-AAGTGCCTATCAAGTGGATGGCATTGG-3' (SEQ ID NO: 930)

5'-UGCCUAUCAAGUGGAUGGCAUUGGA-3' (SEQ ID NO: 1287)
3'-UCACGGAUAGUUCACCUACCGUAACCU-5' (SEQ ID NO: 575)
EGFR-2897 Target: 5'-AGTGCCTATCAAGTGGATGGCATTGGA-3' (SEQ ID NO: 931)

5'-ACCAUCGAUGUCUACAUGAUGG-3' (SEQ ID NO: 1288)
3'-CAUGGUAGCUACAGAUGUACUAGUACC-5' (SEQ ID NO: 576)
EGFR-3088 Target: 5'-GTACCATCGATGTCTACATGATCATGG-3' (SEQ ID NO: 932)

5'-CCAUCGAUGUCUACAUGAUGGU-3' (SEQ ID NO: 1289)
3'-AUGGUAGCUACAGAUGUACUAGUACCA-5' (SEQ ID NO: 577)
EGFR-3089 Target: 5'-TACCATCGATGTCTACATGATCATGGT-3' (SEQ ID NO: 933)

5'-CAUCGAUGUCUACAUGAUGGUC-3' (SEQ ID NO: 1290)
3'-UGGUAGCUACAGAUGUACUAGUACCAG-5' (SEQ ID NO: 578)
EGFR-3090 Target: 5'-ACCATCGATGTCTACATGATCATGGTC-3' (SEQ ID NO: 934)

5'-AUCGAUGUCUACAUGAUGGUCA-3' (SEQ ID NO: 1291)
3'-GGUAGCUACAGAUGUACUAGUACCAGU-5' (SEQ ID NO: 579)
EGFR-3091 Target: 5'-CCATCGATGTCTACATGATCATGGTCA-3' (SEQ ID NO: 935)

5'-UCGAUGUCUACAUGAUGGUCAA-3' (SEQ ID NO: 1292)
3'-GUAGCUACAGAUGUACUAGUACCAGUU-5' (SEQ ID NO: 580)
EGFR-3092 Target: 5'-CATCGATGTCTACATGATCATGGTCAA-3' (SEQ ID NO: 936)

5'-CGAUGUCUACAUGAUGGUCAAG-3' (SEQ ID NO: 1293)
3'-UAGCUACAGAUGUACUAGUACCAGUUC-5' (SEQ ID NO: 581)
EGFR-3093 Target: 5'-ATCGATGTCTACATGATCATGGTCAAG-3' (SEQ ID NO: 937)

5'-GAUGUCUACAUGAUGGUCAAGU-3' (SEQ ID NO: 1294)
3'-AGCUACAGAUGUACUAGUACCAGUUCA-5' (SEQ ID NO: 582)
EGFR-3094 Target: 5'-TCGATGTCTACATGATCATGGTCAAGT-3' (SEQ ID NO: 938)

5'-AUGUCUACAUGAUGGUCAAGUG-3' (SEQ ID NO: 1295)
3'-GCUACAGAUGUACUAGUACCAGUUCAC-5' (SEQ ID NO: 583)
EGFR-3095 Target: 5'-CGATGTCTACATGATCATGGTCAAGTG-3' (SEQ ID NO: 939)

5'-UGUCUACAUGAUGGUCAAGUGC-3' (SEQ ID NO: 1296)
3'-CUACAGAUGUACUAGUACCAGUUCACG-5' (SEQ ID NO: 584)
EGFR-3096 Target: 5'-GATGTCTACATGATCATGGTCAAGTGC-3' (SEQ ID NO: 940)

5'-GUCUACAUGAUGGUCAAGUGCU-3' (SEQ ID NO: 1297)
3'-UACAGAUGUACUAGUACCAGUUCACGA-5' (SEQ ID NO: 585)
EGFR-3097 Target: 5'-ATGTCTACATGATCATGGTCAAGTGCT-3' (SEQ ID NO: 941)

5'-UCUACAUGAUGGUCAAGUGCUG-3' (SEQ ID NO: 1298)
3'-ACAGAUGUACUAGUACCAGUUCACGAC-5' (SEQ ID NO: 586)
EGFR-3098 Target: 5'-TGTCTACATGATCATGGTCAAGTGCTG-3' (SEQ ID NO: 942)

5'-CUACAUGAUGGUCAAGUGCUGG-3' (SEQ ID NO: 1299)
3'-CAGAUGUACUAGUACCAGUUCACGACC-5' (SEQ ID NO: 587)
EGFR-3099 Target: 5'-GTCTACATGATCATGGTCAAGTGCTGG-3' (SEQ ID NO: 943)

5'-UACAUGAUGAUGGUCAAGUGCUGGA-3' (SEQ ID NO: 1300)
3'-AGAUGUACUAGUACCAGUUCACGACCU-5' (SEQ ID NO: 588)
EGFR-3100 Target: 5'-TCTACATGATCATGGTCAAGTGCTGGA-3' (SEQ ID NO: 944)

5'-ACAUGAUGAUGGUCAAGUGCUGGAU-3' (SEQ ID NO: 1301)
3'-GAUGUACUAGUACCAGUUCACGACCUA-5' (SEQ ID NO: 589)
EGFR-3101 Target: 5'-CTACATGATCATGGTCAAGTGCTGGAT-3' (SEQ ID NO: 945)

5'-CAUGAUGAUGGUCAAGUGCUGGAUG-3' (SEQ ID NO: 1302)
3'-AUGUACUAGUACCAGUUCACGACCUAC-5' (SEQ ID NO: 590)
EGFR-3102 Target: 5'-TACATGATCATGGTCAAGTGCTGGATG-3' (SEQ ID NO: 946)

5'-AUGAUGAUGGUCAAGUGCUGGAUGA-3' (SEQ ID NO: 1303)
3'-UGUACUAGUACCAGUUCACGACCUACU-5' (SEQ ID NO: 591)
EGFR-3103 Target: 5'-ACATGATCATGGTCAAGTGCTGGATGA-3' (SEQ ID NO: 947)

5'-UGAUGAUGGUCAAGUGCUGGAUGAU-3' (SEQ ID NO: 1304)
3'-GUACUAGUACCAGUUCACGACCUACUA-5' (SEQ ID NO: 592)
EGFR-3104 Target: 5'-CATGATCATGGTCAAGTGCTGGATGAT-3' (SEQ ID NO: 948)

5'-GAUGAUGGUCAAGUGCUGGAUGAUA-3' (SEQ ID NO: 1305)
3'-UACUAGUACCAGUUCACGACCUACUAU-5' (SEQ ID NO: 593)
EGFR-3105 Target: 5'-ATGATCATGGTCAAGTGCTGGATGATA-3' (SEQ ID NO: 949)

5'-AUGAUGGUCAAGUGCUGGAUGAUAG-3' (SEQ ID NO: 1306)
3'-ACUAGUACCAGUUCACGACCUACUAUC-5' (SEQ ID NO: 594)
EGFR-3106 Target: 5'-TGATCATGGTCAAGTGCTGGATGATAG-3' (SEQ ID NO: 950)

5'-UCAUGGUCAAGUGCUGGAUGAUAGA-3' (SEQ ID NO: 1307)
3'-CUAGUACCAGUUCACGACCUACUAUCU-5' (SEQ ID NO: 595)
EGFR-3107 Target: 5'-GATCATGGTCAAGTGCTGGATGATAGA-3' (SEQ ID NO: 951)

5'-CAUGGUCAAGUGCUGGAUGAUAGAC-3' (SEQ ID NO: 1308)
3'-UAGUACCAGUUCACGACCUACUAUCUG-5' (SEQ ID NO: 596)
EGFR-3108 Target: 5'-ATCATGGTCAAGTGCTGGATGATAGAC-3' (SEQ ID NO: 952)

5'-AUGGUCAAGUGCUGGAUGAUAGACG-3' (SEQ ID NO: 1309)
3'-AGUACCAGUUCACGACCUACUAUCUGC-5' (SEQ ID NO: 597)
EGFR-3109 Target: 5'-TCATGGTCAAGTGCTGGATGATAGACG-3' (SEQ ID NO: 953)

5'-UGGUCAAGUGCUGGAUGAUAGACGC-3' (SEQ ID NO: 1310)
3'-GUACCAGUUCACGACCUACUAUCUGCG-5' (SEQ ID NO: 598)
EGFR-3110 Target: 5'-CATGGTCAAGTGCTGGATGATAGACGC-3' (SEQ ID NO: 954)

5'-GGUCAAGUGCUGGAUGAUAGACGCA-3' (SEQ ID NO: 1311)
3'-UACCAGUUCACGACCUACUAUCUGCGU-5' (SEQ ID NO: 599)

EGFR-3111 Target: 5'-ATGGTCAAGTGCTGGATGATAGACGCA-3' (SEQ ID NO: 955)

5'-GUCAAGUGCUGGAUGAUAGACGCAG-3' (SEQ ID NO: 1312)

3'-ACCAGUUCACGACCUACUAUCUGCGUC-5' (SEQ ID NO: 600)

EGFR-3112 Target: 5'-TGGTCAAGTGCTGGATGATAGACGCAG-3' (SEQ ID NO: 956)

5'-UCAAGUGCUGGAUGAUAGACGCAGA-3' (SEQ ID NO: 1313)

3'-CCAGUUCACGACCUACUAUCUGCGUCU-5' (SEQ ID NO: 601)

EGFR-3113 Target: 5'-GGTCAAGTGCTGGATGATAGACGCAGA-3' (SEQ ID NO: 957)

5'-GAAUUCUCCAAAAUGGCCCCGAGACC-3' (SEQ ID NO: 1314)

3'-AGCUUAAGAGGUUUUACCGGCUCUGG-5' (SEQ ID NO: 602)

EGFR-3169 Target: 5'-TCGAATTCTCCAAAATGGCCCCGAGACC-3' (SEQ ID NO: 958)

5'-AAUUCUCCAAAAUGGCCCCGAGACCC-3' (SEQ ID NO: 1315)

3'-GCUUAAGAGGUUUUACCGGCUCUGGG-5' (SEQ ID NO: 603)

EGFR-3170 Target: 5'-CGAATTCTCCAAAATGGCCCCGAGACCC-3' (SEQ ID NO: 959)

5'-GAUGAAAGAAUGCAUUUGCCAAGUC-3' (SEQ ID NO: 1316)

3'-CCCUCUUUUACGUAAACGGUUCAG-5' (SEQ ID NO: 604)

EGFR-3220 Target: 5'-GGGATGAAAGAATGCATTTGCCAAGTC-3' (SEQ ID NO: 960)

5'-AUGAAAGAAUGCAUUUGCCAAGUCC-3' (SEQ ID NO: 1317)

3'-CCUACUUUUACGUAAACGGUUCAGG-5' (SEQ ID NO: 605)

EGFR-3221 Target: 5'-GGATGAAAGAATGCATTTGCCAAGTCC-3' (SEQ ID NO: 961)

5'-UGAAAGAAUGCAUUUGCCAAGUCCU-3' (SEQ ID NO: 1318)

3'-CUACUUUUACGUAAACGGUUCAGGA-5' (SEQ ID NO: 606)

EGFR-3222 Target: 5'-GATGAAAGAATGCATTTGCCAAGTCCT-3' (SEQ ID NO: 962)

5'-GAAAGAAUGCAUUUGCCAAGUCCUA-3' (SEQ ID NO: 1319)

3'-UACUUUUUUACGUAAACGGUUCAGGAU-5' (SEQ ID NO: 607)

EGFR-3223 Target: 5'-ATGAAAGAATGCATTTGCCAAGTCCTA-3' (SEQ ID NO: 963)

5'-AAAGAAUGCAUUUGCCAAGUCCUAC-3' (SEQ ID NO: 1320)

3'-ACUUUUUUACGUAAACGGUUCAGGAUG-5' (SEQ ID NO: 608)

EGFR-3224 Target: 5'-TGAAAGAATGCATTTGCCAAGTCCTAC-3' (SEQ ID NO: 964)

5'-GACAACCCUGACUACCAGCAGGACU-3' (SEQ ID NO: 1321)

3'-ACCUGUUGGGACUGAUGGUCGUCCUGA-5' (SEQ ID NO: 609)

EGFR-3772 Target: 5'-TGGACAACCCTGACTACCAGCAGGACT-3' (SEQ ID NO: 965)

5'-ACAACCCUGACUACCAGCAGGACUU-3' (SEQ ID NO: 1322)

3'-CCUGUUGGGACUGAUGGUCGUCCUGAA-5' (SEQ ID NO: 610)

EGFR-3773 Target: 5'-GGACAACCCCTGACTACCAGCAGGACTT-3' (SEQ ID NO: 966)

5'-CAACCCUGACUACCAGCAGGACUUC-3' (SEQ ID NO: 1323)

3'-CUGUUGGGACUGAUGGUCGUCCUGAAG-5' (SEQ ID NO: 611)
 EGFR-3774 Target: 5'-GACAACCCTGACTACCAGCAGGACTTC-3' (SEQ ID NO: 967)

5'-AACCCUGACUACCAGCAGGACUUCU-3' (SEQ ID NO: 1324)
 3'-UGUUGGGACUGAUGGUCGUCCUGAAGA-5' (SEQ ID NO: 612)
 EGFR-3775 Target: 5'-ACAACCCTGACTACCAGCAGGACTTCT-3' (SEQ ID NO: 968)

5'-ACCCUGACUACCAGCAGGACUUCUU-3' (SEQ ID NO: 1325)
 3'-GUUGGGACUGAUGGUCGUCCUGAAGAA-5' (SEQ ID NO: 613)
 EGFR-3776 Target: 5'-CAACCCTGACTACCAGCAGGACTTCTT-3' (SEQ ID NO: 969)

5'-CCCUGACUACCAGCAGGACUUCUUU-3' (SEQ ID NO: 1326)
 3'-UUGGGACUGAUGGUCGUCCUGAAGAAA-5' (SEQ ID NO: 614)
 EGFR-3777 Target: 5'-AACCCCTGACTACCAGCAGGACTTCTTT-3' (SEQ ID NO: 970)

5'-CCUGACUACCAGCAGGACUUCUUUC-3' (SEQ ID NO: 1327)
 3'-UGGGACUGAUGGUCGUCCUGAAGAAAAG-5' (SEQ ID NO: 615)
 EGFR-3778 Target: 5'-ACCCTGACTACCAGCAGGACTTCTTTC-3' (SEQ ID NO: 971)

5'-CUGACUACCAGCAGGACUUCUUUCC-3' (SEQ ID NO: 1328)
 3'-GGGACUGAUGGUCGUCCUGAAGAAAGG-5' (SEQ ID NO: 616)
 EGFR-3779 Target: 5'-CCCTGACTACCAGCAGGACTTCTTTCC-3' (SEQ ID NO: 972)

Table 4: Selected Mouse Anti-EGFR DsiRNAs (Asymmetrics)

5'-GCGCAACGCGCAGCAGCCUCCCUcc-3' (SEQ ID NO: 261)
 3'-GUCGCGUUGCGGUCGUCGGAGGGAGG-5' (SEQ ID NO: 617)
 EGFR-m71 Target: 5'-CAGCGCAACGCGCAGCAGCCTCCCTCC-3' (SEQ ID NO: 973)

5'-GCGCAGCAGCCUCCCUCCUCUUCtt-3' (SEQ ID NO: 262)
 3'-UGCGCGUCGUCGGAGGGAGGAGAAGAA-5' (SEQ ID NO: 618)
 EGFR-m78 Target: 5'-ACGCGCAGCAGCCTCCCTCCTTCTT-3' (SEQ ID NO: 974)

5'-CCUCCUCCUCUUCUCCCCGCActg-3' (SEQ ID NO: 263)
 3'-UCGGAGGGAGGAGAAGAAGGGCGUGAC-5' (SEQ ID NO: 619)
 EGFR-m87 Target: 5'-AGCCTCCCTCCTTCTTCCCGCACTG-3' (SEQ ID NO: 975)

5'-CCUCCUCCUCUUCUCCCCGCACUGUgc-3' (SEQ ID NO: 264)
 3'-GAGGGAGGAGAAGAAGGGCGUGACACG-5' (SEQ ID NO: 620)
 EGFR-m90 Target: 5'-CTCCCTCCTTCTTCCCGCACTGTGC-3' (SEQ ID NO: 976)

5'-CUCCUCCUCUUCUCCCCGCACUGUGCgc-3' (SEQ ID NO: 265)
 3'-GGGAGGAGAAGAAGGGCGUGACACGCG-5' (SEQ ID NO: 621)
 EGFR-m92 Target: 5'-CCCTCCTTCTTCCCGCACTGTGCGC-3' (SEQ ID NO: 977)

5'-CCUCUCCUUCUCCCCGCACUGUGCGctc-3' (SEQ ID NO: 266)

3'-GAGGAAGAAGGGCGUGACACGCGAG-5' (SEQ ID NO: 622)
EGFR-m94 Target: 5'-CTCCTCTTCTTCCCGCACTGTGCGCTC-3' (SEQ ID NO: 978)

5'-CUUCUCCCCGCACUGUGCGCUCCt-3' (SEQ ID NO: 267)
3'-GAGAAAGAAGGGCGUGACACGCGAGGAG-5' (SEQ ID NO: 623)
EGFR-m97 Target: 5'-CTCTTCTTCCCGCACTGTGCGCTCCTC-3' (SEQ ID NO: 979)

5'-UCUCCCCGCACUGUGCGCUCCUCt-3' (SEQ ID NO: 268)
3'-GAGAAAGGGCGUGACACGCGAGGAGGA-5' (SEQ ID NO: 624)
EGFR-m99 Target: 5'-CTTCTTCCCGCACTGTGCGCTCCTCCT-3' (SEQ ID NO: 980)

5'-CUUCCCCGCACUGUGCGCUCCUCtg-3' (SEQ ID NO: 269)
3'-AAGAAGGGCGUGACACGCGAGGAGGAC-5' (SEQ ID NO: 625)
EGFR-m100 Target: 5'-TTCTTCCCGCACTGTGCGCTCCTCCTG-3' (SEQ ID NO: 981)

5'-UUCCCCGCACUGUGCGCUCCUCCUgg-3' (SEQ ID NO: 270)
3'-AGAAAGGGCGUGACACGCGAGGAGGACC-5' (SEQ ID NO: 626)
EGFR-m101 Target: 5'-TCTTCCCGCACTGTGCGCTCCTCCTGG-3' (SEQ ID NO: 982)

5'-GUGCGCUCCUCCUGGGCUAGGGCgt-3' (SEQ ID NO: 271)
3'-GACACGCGAGGAGGACCCGAUCCCGCA-5' (SEQ ID NO: 627)
EGFR-m111 Target: 5'-CTGTGCGCTCCTCCTGGGCTAGGGCGT-3' (SEQ ID NO: 983)

5'-CGCUCCUCCUGGGCUAGGGCGUctg-3' (SEQ ID NO: 272)
3'-ACGCGAGGAGGACCCGAUCCCGCAGAC-5' (SEQ ID NO: 628)
EGFR-m114 Target: 5'-TGCGCTCCTCCTGGGCTAGGGCGTCTG-3' (SEQ ID NO: 984)

5'-CACUGCUGGUGUUGCUGACCGCGct-3' (SEQ ID NO: 273)
3'-GUGUGACGACCACAACGACUGGCGCGA-5' (SEQ ID NO: 629)
EGFR-m333 Target: 5'-CACACTGCTGGTGTGCTGACCGCGCT-3' (SEQ ID NO: 985)

5'-ACUGCUGGUGUUGCUGACCGCGCtc-3' (SEQ ID NO: 274)
3'-UGUGACGACCACAACGACUGGCGCGAG-5' (SEQ ID NO: 630)
EGFR-m334 Target: 5'-ACACTGCTGGTGTGCTGACCGCGCTC-3' (SEQ ID NO: 986)

5'-CUGCUGGUGUUGCUGACCGCGCUct-3' (SEQ ID NO: 275)
3'-GUGACGACCACAACGACUGGCGCGAGA-5' (SEQ ID NO: 631)
EGFR-m335 Target: 5'-CACTGCTGGTGTGCTGACCGCGCTCT-3' (SEQ ID NO: 987)

5'-UGCUGGUGUUGCUGACCGCGCUctg-3' (SEQ ID NO: 276)
3'-UGACGACCACAACGACUGGCGCGAGAC-5' (SEQ ID NO: 632)
EGFR-m336 Target: 5'-ACTGCTGGTGTGCTGACCGCGCTCTG-3' (SEQ ID NO: 988)

5'-GCUGGUGUUGCUGACCGCGCUCUgc-3' (SEQ ID NO: 277)
3'-GACGACCACAACGACUGGCGCGAGACG-5' (SEQ ID NO: 633)
EGFR-m337 Target: 5'-CTGCTGGTGTGCTGACCGCGCTCTGC-3' (SEQ ID NO: 989)

5'-CUGGUGUUGCUGACCGCGCUCUGcg-3' (SEQ ID NO: 278)
3'-ACGACCACAACGACUGGCGCGAGACGC-5' (SEQ ID NO: 634)
EGFR-m338 Target: 5'-TGCTGGTGTGCTGACCGCGCTCTGCG-3' (SEQ ID NO: 990)

5'-UGGUGUUGCUGACCGCGCUCUGCgc-3' (SEQ ID NO: 279)
3'-CGACCACAACGACUGGCGCGAGACGCG-5' (SEQ ID NO: 635)
EGFR-m339 Target: 5'-GCTGGTGTGCTGACCGCGCTCTGCGC-3' (SEQ ID NO: 991)

5'-GUGUUGCUGACCGCGCUCUGCGCcg-3' (SEQ ID NO: 280)
3'-ACCACAACGACUGGCGCGAGACGCGGC-5' (SEQ ID NO: 636)
EGFR-m341 Target: 5'-TGGTGTGCTGACCGCGCTCTGCGCCG-3' (SEQ ID NO: 992)

5'-UGUUGCUGACCGCGCUCUGCGCCgc-3' (SEQ ID NO: 281)
3'-CCACAACGACUGGCGCGAGACGCGGCG-5' (SEQ ID NO: 637)
EGFR-m342 Target: 5'-GGTGTGCTGACCGCGCTCTGCGCCGC-3' (SEQ ID NO: 993)

5'-GUUGCUGACCGCGCUCUGCGCCGca-3' (SEQ ID NO: 282)
3'-CACAACGACUGGCGCGAGACGCGGCGU-5' (SEQ ID NO: 638)
EGFR-m343 Target: 5'-GTGTTGCTGACCGCGCTCTGCGCCGCA-3' (SEQ ID NO: 994)

5'-UUGCUGACCGCGCUCUGCGCCGCag-3' (SEQ ID NO: 283)
3'-ACAACGACUGGCGCGAGACGCGGCGUC-5' (SEQ ID NO: 639)
EGFR-m344 Target: 5'-TGTTGCTGACCGCGCTCTGCGCCGCAG-3' (SEQ ID NO: 995)

5'-CUGACCGCGCUCUGCGCCGCAGgt-3' (SEQ ID NO: 284)
3'-ACGACUGGCGCGAGACGCGGCGUCCAC-5' (SEQ ID NO: 640)
EGFR-m347 Target: 5'-TGCTGACCGCGCTCTGCGCCGCAGGTG-3' (SEQ ID NO: 996)

5'-UGACCGCGCUCUGCGCCGCAGGUgg-3' (SEQ ID NO: 285)
3'-CGACUGGCGCGAGACGCGGCGUCCACC-5' (SEQ ID NO: 641)
EGFR-m348 Target: 5'-GCTGACCGCGCTCTGCGCCGCAGGTGG-3' (SEQ ID NO: 997)

5'-CUGAUUGGUGCUGUGCGAUUCAGca-3' (SEQ ID NO: 286)
3'-AGGACUAACCACGACACGCUAAGUCGU-5' (SEQ ID NO: 642)
EGFR-m734 Target: 5'-TCCTGATTGGTGCTGTGCGATTGAGCA-3' (SEQ ID NO: 998)

5'-UGAUUGGUGCUGUGCGAUUCAGCaa-3' (SEQ ID NO: 287)
3'-GGACUAACCACGACACGCUAAGUCGUU-5' (SEQ ID NO: 643)
EGFR-m735 Target: 5'-CCTGATTGGTGCTGTGCGATTGAGCAA-3' (SEQ ID NO: 999)

5'-GAUUGGUGCUGUGCGAUUCAGCAac-3' (SEQ ID NO: 288)
3'-GACUAACCACGACACGCUAAGUCGUUG-5' (SEQ ID NO: 644)
EGFR-m736 Target: 5'-CTGATTGGTGCTGTGCGATTGAGCAAC-3' (SEQ ID NO: 1000)

5'-UUGGUGCUGUGCGAUUCAGCAACaa-3' (SEQ ID NO: 289)
3'-CUAACCACGACACGCUAAGUCGUUGU-5' (SEQ ID NO: 645)
EGFR-m738 Target: 5'-GATTGGTGCTGTGCGATTGAGCAACAA-3' (SEQ ID NO: 1001)

5'-GGUGCUGUGCGAUUCAGCAACAACc-3' (SEQ ID NO: 290)
3'-AACCACGACACGCUAAGUCGUUGUUGG-5' (SEQ ID NO: 646)
EGFR-m740 Target: 5'-TTGGTGCTGTGCGATTGAGCAACAACC-3' (SEQ ID NO: 1002)

5'-GUGCUGUGCGAUUCAGCAACAACcc-3' (SEQ ID NO: 291)
3'-ACCACGACACGCUAAGUCGUUGUUGGG-5' (SEQ ID NO: 647)
EGFR-m741 Target: 5'-TGGTGCTGTGCGATTGAGCAACAACCC-3' (SEQ ID NO: 1003)

5'-CAAGCUGUCCCAAUGGAAGCUGCtg-3' (SEQ ID NO: 292)
3'-AGGUUCGACAGGGUUAACCUUCGACGAC-5' (SEQ ID NO: 648)
EGFR-m879 Target: 5'-TCCAAGCTGTCCCAATGGAAGCTGCTG-3' (SEQ ID NO: 1004)

5'-GUGCCCAGCAAUGUCCCCAUCGCTg-3' (SEQ ID NO: 293)
3'-GACACGGGUCGUUACAAGGGUAGCGAC-5' (SEQ ID NO: 649)
EGFR-m948 Target: 5'-CTGTGCCCGAGCAATGTTCCCATCGCTG-3' (SEQ ID NO: 1005)

5'-AAGUACAGCUUUGGUGCCACCUGtg-3' (SEQ ID NO: 294)
3'-CCUUAUGUCGAAACCACGGUGGACAC-5' (SEQ ID NO: 650)
EGFR-m1154 Target: 5'-GGAAGTACAGCTTTGGTGCCACCTGTG-3' (SEQ ID NO: 1006)

5'-GUCGCAAAGUUUGUAAUGGCAUAgg-3' (SEQ ID NO: 295)
3'-GACAGCGUUUCAAACAUUACCGUAUCC-5' (SEQ ID NO: 651)
EGFR-m1302 Target: 5'-CTGTCGCAAAGTTTGTAATGGCATAGG-3' (SEQ ID NO: 1007)

5'-GAUUCUUUCACGCGCACUCCUCctc-3' (SEQ ID NO: 296)
3'-CCCUAAGAAAGUGCGCGUGAGGAGGAG-5' (SEQ ID NO: 652)
EGFR-m1439 Target: 5'-GGGATTCTTTCACGCGCACTCCTCCTC-3' (SEQ ID NO: 1008)

5'-CAGGCUUUUUGCUGAUUCAGGCUtg-3' (SEQ ID NO: 297)
3'-UUGUCCGAAAAACGACUAAGUCCGAAC-5' (SEQ ID NO: 653)
EGFR-m1509 Target: 5'-AACAGGCTTTTTTGCTGATTGAGGCTTG-3' (SEQ ID NO: 1009)

5'-CAGGCUUGGCCUGAUAAACUGGACTg-3' (SEQ ID NO: 298)
3'-AAGUCCGAACCGGACUAUUGACCUGAC-5' (SEQ ID NO: 654)
EGFR-m1526 Target: 5'-TTCAGGCTTGGCCTGATAACTGGACTG-3' (SEQ ID NO: 1010)

5'-GGCUUGGCCUGAUAAACUGGACUGac-3' (SEQ ID NO: 299)
3'-GUCCGAACCGGACUAUUGACCUGACUG-5' (SEQ ID NO: 655)
EGFR-m1528 Target: 5'-CAGGCTTGGCCTGATAACTGGACTGAC-3' (SEQ ID NO: 1011)

5'-UUGGCCUGAUAAACUGGACUGACctc-3' (SEQ ID NO: 300)
3'-CGAACCGGACUAUUGACCUGACUGGAG-5' (SEQ ID NO: 656)
EGFR-m1531 Target: 5'-GCTTGGCCTGATAACTGGACTGACCTC-3' (SEQ ID NO: 1012)

5'-GCCAACUGUACCUAUGGAUGUGCtg-3' (SEQ ID NO: 301)
3'-UGCGGUUGACAUGGAUACCUACACGAC-5' (SEQ ID NO: 657)

EGFR-m2168 Target: 5'-ACGCCAACTGTACCTATGGATGTGCTG-3' (SEQ ID NO: 1013)

5'-CUGGGAUUGUGGGUGGCCUCCUctt-3' (SEQ ID NO: 302)

3'-GUGACCCUAACACCCACCGGAGGAGAA-5' (SEQ ID NO: 658)

EGFR-m2253 Target: 5'-CACTGGGATTGTGGGTGGCCTCCTCTT-3' (SEQ ID NO: 1014)

5'-UGGUGGCCCCUUGGGAUUGGCCUAtt-3' (SEQ ID NO: 303)

3'-CCACCACCGGGAACCCUAACCGGAUAA-5' (SEQ ID NO: 659)

EGFR-m2286 Target: 5'-GGTGGTGGCCCTTGGGATTGGCCTATT-3' (SEQ ID NO: 1015)

5'-UUGGCCUAUUCAUGCGAAGACGUca-3' (SEQ ID NO: 304)

3'-CUAACCGGAUAAGUACGCUUCUGCAGU-5' (SEQ ID NO: 660)

EGFR-m2301 Target: 5'-GATTGGCCTATTTCATGCGAAGACGTCA-3' (SEQ ID NO: 1016)

5'-CCGCCUGCUUCAAGAGAGAGAGCtc-3' (SEQ ID NO: 305)

3'-GCGGCGGACGAAGUUCUCUCUCUCGAG-5' (SEQ ID NO: 661)

EGFR-m2350 Target: 5'-CGCCGCCTGCTTCAAGAGAGAGAGCTC-3' (SEQ ID NO: 1017)

5'-CGCCUGCUUCAAGAGAGAGAGCUcg-3' (SEQ ID NO: 306)

3'-CGGCGGACGAAGUUCUCUCUCUCGAGC-5' (SEQ ID NO: 662)

EGFR-m2351 Target: 5'-GCCGCCTGCTTCAAGAGAGAGAGCTCG-3' (SEQ ID NO: 1018)

5'-GCCUGCUUCAAGAGAGAGAGCUCgt-3' (SEQ ID NO: 307)

3'-GGCGGACGAAGUUCUCUCUCUCGAGCA-5' (SEQ ID NO: 663)

EGFR-m2352 Target: 5'-CCGCCTGCTTCAAGAGAGAGAGCTCGT-3' (SEQ ID NO: 1019)

5'-GGACAACCCUCAUGUAUGCCGCctc-3' (SEQ ID NO: 308)

3'-CACCUGUUGGGAGUACAUACGGCGGAG-5' (SEQ ID NO: 664)

EGFR-m2617 Target: 5'-GTGGACAACCCCTCATGTATGCCGCCTC-3' (SEQ ID NO: 1020)

5'-UAUGCCGCCUCCUGGGCAUCUGUct-3' (SEQ ID NO: 309)

3'-ACAUACGGCGGAGGACCCGUAGACAGA-5' (SEQ ID NO: 665)

EGFR-m2631 Target: 5'-TGTATGCCGCCTCCTGGGCATCTGTCT-3' (SEQ ID NO: 1021)

5'-GCUCAUGCCCUACGGUUGCCUCctg-3' (SEQ ID NO: 310)

3'-GUCGAGUACGGGAUGCCAACGGAGGAC-5' (SEQ ID NO: 666)

EGFR-m2683 Target: 5'-CAGCTCATGCCCTACGGTTGCCTCCTG-3' (SEQ ID NO: 1022)

5'-CUCAUGCCCUACGGUUGCCUCCUgg-3' (SEQ ID NO: 311)

3'-UCGAGUACGGGAUGCCAACGGAGGACC-5' (SEQ ID NO: 667)

EGFR-m2684 Target: 5'-AGCTCATGCCCTACGGTTGCCTCCTGG-3' (SEQ ID NO: 1023)

5'-UCGGCGUUUGGUGCACCGUGACUtg-3' (SEQ ID NO: 312)

3'-CUAGCCGCAAACACGUGGCACUGAAC-5' (SEQ ID NO: 668)

EGFR-m2800 Target: 5'-GATCGGCGTTTGGTGCACCGTGACTTG-3' (SEQ ID NO: 1024)

5'-GUUUGGUGCACCGUGACUUGGCAGc-3' (SEQ ID NO: 313)

3'-CGCAAACCACGUGGCACUGAACCGUCG-5' (SEQ ID NO: 669)
EGFR-m2805 Target: 5'-GCGTTTGGTGCAACCGTGGCAGC-3' (SEQ ID NO: 1025)

5'-GGGCUGGCCAAACUGCUUGGUGCtg-3' (SEQ ID NO: 314)
3'-AACCCGACCGGUUUGACGAACCACGAC-5' (SEQ ID NO: 670)
EGFR-m2879 Target: 5'-TTGGGCTGGCCAAACTGCTTGGTGCTG-3' (SEQ ID NO: 1026)

5'-GGCUGGCCAAACUGCUUGGUGCUga-3' (SEQ ID NO: 315)
3'-ACCCGACCGGUUUGACGAACCACGACU-5' (SEQ ID NO: 671)
EGFR-m2880 Target: 5'-TGGGCTGGCCAAACTGCTTGGTGCTGA-3' (SEQ ID NO: 1027)

5'-CUGGCCAAACUGCUUGGUGCUGAag-3' (SEQ ID NO: 316)
3'-CCGACCGGUUUGACGAACCACGACUUC-5' (SEQ ID NO: 672)
EGFR-m2882 Target: 5'-GGCTGGCCAAACTGCTTGGTGCTGAAG-3' (SEQ ID NO: 1028)

5'-UGGCCAAACUGCUUGGUGCUGAAga-3' (SEQ ID NO: 317)
3'-CGACCGGUUUGACGAACCACGACUUCU-5' (SEQ ID NO: 673)
EGFR-m2883 Target: 5'-GCTGGCCAAACTGCTTGGTGCTGAAGA-3' (SEQ ID NO: 1029)

5'-CAAGUGCUGGAUGAUAGAUGCUGat-3' (SEQ ID NO: 318)
3'-CAGUUCACGACCUACUAUCUACGACUA-5' (SEQ ID NO: 674)
EGFR-m3154 Target: 5'-GTCAAGTGCTGGATGATAGATGCTGAT-3' (SEQ ID NO: 1030)

5'-AAGUGCUGGAUGAUAGAUGCUGAta-3' (SEQ ID NO: 319)
3'-AGUUCACGACCUACUAUCUACGACUAU-5' (SEQ ID NO: 675)
EGFR-m3155 Target: 5'-TCAAGTGCTGGATGATAGATGCTGATA-3' (SEQ ID NO: 1031)

5'-AGUGCUGGAUGAUAGAUGCUGAUag-3' (SEQ ID NO: 320)
3'-GUUACGACCUACUAUCUACGACUAUC-5' (SEQ ID NO: 676)
EGFR-m3156 Target: 5'-CAAGTGCTGGATGATAGATGCTGATAG-3' (SEQ ID NO: 1032)

5'-GUGCUGGAUGAUAGAUGCUGAUAgc-3' (SEQ ID NO: 321)
3'-UUCACGACCUACUAUCUACGACUAUCG-5' (SEQ ID NO: 677)
EGFR-m3157 Target: 5'-AAGTGCTGGATGATAGATGCTGATAGC-3' (SEQ ID NO: 1033)

5'-UGCUGGAUGAUAGAUGCUGAUAGcc-3' (SEQ ID NO: 322)
3'-UCACGACCUACUAUCUACGACUAUCGG-5' (SEQ ID NO: 678)
EGFR-m3158 Target: 5'-AGTGCTGGATGATAGATGCTGATAGCC-3' (SEQ ID NO: 1034)

5'-GCUGGAUGAUAGAUGCUGAUAGCcg-3' (SEQ ID NO: 323)
3'-CACGACCUACUAUCUACGACUAUCGGC-5' (SEQ ID NO: 679)
EGFR-m3159 Target: 5'-GTGCTGGATGATAGATGCTGATAGCCG-3' (SEQ ID NO: 1035)

5'-CUGGAUGAUAGAUGCUGAUAGCCgc-3' (SEQ ID NO: 324)
3'-ACGACCUACUAUCUACGACUAUCGGCG-5' (SEQ ID NO: 680)
EGFR-m3160 Target: 5'-TGCTGGATGATAGATGCTGATAGCCGC-3' (SEQ ID NO: 1036)

5'-UGGAUGAUAGAUGCUGAUAGCCGcc-3' (SEQ ID NO: 325)
3'-CGACCUACUAUCUACGACUAUCGGCGG-5' (SEQ ID NO: 681)
EGFR-m3161 Target: 5'-GCTGGATGATAGATGCTGATAGCCGCC-3' (SEQ ID NO: 1037)

5'-GGAUGAUAGAUGCUGAUAGCCGcc-3' (SEQ ID NO: 326)
3'-GACCUACUAUCUACGACUAUCGGCGGG-5' (SEQ ID NO: 682)
EGFR-m3162 Target: 5'-CTGGATGATAGATGCTGATAGCCGCCC-3' (SEQ ID NO: 1038)

5'-GAUGAUAGAUGCUGAUAGCCGCCca-3' (SEQ ID NO: 327)
3'-ACCUACUAUCUACGACUAUCGGCGGGU-5' (SEQ ID NO: 683)
EGFR-m3163 Target: 5'-TGGATGATAGATGCTGATAGCCGCCCA-3' (SEQ ID NO: 1039)

5'-GAUAGAUGCUGAUAGCCGCCCAag-3' (SEQ ID NO: 328)
3'-UACUACUAUCGACUAUCGGCGGGUUUC-5' (SEQ ID NO: 684)
EGFR-m3166 Target: 5'-ATGATAGATGCTGATAGCCGCCCAAAG-3' (SEQ ID NO: 1040)

5'-UAGAUGCUGAUAGCCGCCCAAAGtt-3' (SEQ ID NO: 329)
3'-CUAUCUACGACUAUCGGCGGGUUUCA-5' (SEQ ID NO: 685)
EGFR-m3168 Target: 5'-GATAGATGCTGATAGCCGCCCAAAGTT-3' (SEQ ID NO: 1041)

5'-GCUGCCGUGUCAAAAGAAGACGCctt-3' (SEQ ID NO: 330)
3'-CUCGACGGCACAGUUUCUUCUGCGGAA-5' (SEQ ID NO: 686)
EGFR-m3474 Target: 5'-GAGCTGCCGTGTCAAAGAAGACGCCTT-3' (SEQ ID NO: 1042)

5'-CUGCCGUGUCAAAAGAAGACGCCUtc-3' (SEQ ID NO: 331)
3'-UCGACGGCACAGUUUCUUCUGCGGAAG-5' (SEQ ID NO: 687)
EGFR-m3475 Target: 5'-AGCTGCCGTGTCAAAGAAGACGCCTTC-3' (SEQ ID NO: 1043)

5'-GACGCCUUCUUGCAGCGGUACAGct-3' (SEQ ID NO: 332)
3'-UUCUGCGGAAGAACGUCGCCAUGUCGA-5' (SEQ ID NO: 688)
EGFR-m3491 Target: 5'-AAGACGCCTTCTTGACGCGGTACAGCT-3' (SEQ ID NO: 1044)

5'-ACGCCUUCUUGCAGCGGUACAGCtc-3' (SEQ ID NO: 333)
3'-UCUGCGGAAGAACGUCGCCAUGUCGAG-5' (SEQ ID NO: 689)
EGFR-m3492 Target: 5'-AGACGCCTTCTTGACGCGGTACAGCTC-3' (SEQ ID NO: 1045)

5'-CGCCUUCUUGCAGCGGUACAGCUcc-3' (SEQ ID NO: 334)
3'-CUCGCGGAAGAACGUCGCCAUGUCGAGG-5' (SEQ ID NO: 690)
EGFR-m3493 Target: 5'-GACGCCTTCTTGACGCGGTACAGCTCC-3' (SEQ ID NO: 1046)

5'-GCCUUCUUGCAGCGGUACAGCUCcg-3' (SEQ ID NO: 335)
3'-UGCGGAAGAACGUCGCCAUGUCGAGGC-5' (SEQ ID NO: 691)
EGFR-m3494 Target: 5'-ACGCCTTCTTGACGCGGTACAGCTCCG-3' (SEQ ID NO: 1047)

5'-CCUUCUUGCAGCGGUACAGCUCCga-3' (SEQ ID NO: 336)
3'-GCGGGAAGAACGUCGCCAUGUCGAGGCU-5' (SEQ ID NO: 692)
EGFR-m3495 Target: 5'-CGCCTTCTTGACGCGGTACAGCTCCGA-3' (SEQ ID NO: 1048)

5'-CUUCUUGCAGCGGUACAGCUCCGac-3' (SEQ ID NO: 337)
3'-CGGAAAGAACGUCGCCAUGUCGAGGCUG-5' (SEQ ID NO: 693)
EGFR-m3496 Target: 5'-GCCTTCTTGCAGCGGTACAGCTCCGAC-3' (SEQ ID NO: 1049)

5'-UUCUUGCAGCGGUACAGCUCCGAcc-3' (SEQ ID NO: 338)
3'-GGAAAGAACGUCGCCAUGUCGAGGCUGG-5' (SEQ ID NO: 694)
EGFR-m3497 Target: 5'-CCTTCTTGCAGCGGTACAGCTCCGACC-3' (SEQ ID NO: 1050)

5'-CUGGCUUUAAAGCAUAACUCUGAtg-3' (SEQ ID NO: 339)
3'-CUGACCGAAAUUUCGUAUUGAGACUAC-5' (SEQ ID NO: 695)
EGFR-m4056 Target: 5'-GACTGGCTTTAAAGCATAACTCTGATG-3' (SEQ ID NO: 1051)

5'-GUGGGCCUCUCUCCUGAUGCACUtt-3' (SEQ ID NO: 340)
3'-UUCACCCCGGAGAGAGGACUACGUGAAA-5' (SEQ ID NO: 696)
EGFR-m4103 Target: 5'-AAGTGGGCCTCTCTCCTGATGCACTTT-3' (SEQ ID NO: 1052)

5'-UGGGCCUCUCUCCUGAUGCACUUtg-3' (SEQ ID NO: 341)
3'-UCACCCCGGAGAGAGGACUACGUGAAAC-5' (SEQ ID NO: 697)
EGFR-m4104 Target: 5'-AGTGGGCCTCTCTCCTGATGCACTTTG-3' (SEQ ID NO: 1053)

5'-GGGCCUCUCUCCUGAUGCACUUUgg-3' (SEQ ID NO: 342)
3'-CACCCCGGAGAGAGGACUACGUGAAACC-5' (SEQ ID NO: 698)
EGFR-m4105 Target: 5'-GTGGGCCTCTCTCCTGATGCACTTTGG-3' (SEQ ID NO: 1054)

5'-GGCCUCUCUCCUGAUGCACUUUGgg-3' (SEQ ID NO: 343)
3'-ACCCCGGAGAGAGGACUACGUGAAACCC-5' (SEQ ID NO: 699)
EGFR-m4106 Target: 5'-TGGGCCTCTCTCCTGATGCACTTTGGG-3' (SEQ ID NO: 1055)

5'-CUCUCUCCUGAUGCACUUUGGAag-3' (SEQ ID NO: 344)
3'-CGGAGAGAGGACUACGUGAAACCCUUC-5' (SEQ ID NO: 700)
EGFR-m4109 Target: 5'-GCCTCTCTCCTGATGCACTTTGGGAAG-3' (SEQ ID NO: 1056)

5'-UUGAUGCACUCUUGUAGUCUGGUac-3' (SEQ ID NO: 345)
3'-CUAACUACGUGAGAACAUCAAGACCAUG-5' (SEQ ID NO: 701)
EGFR-m4309 Target: 5'-GATTGATGCACTCTTGTAAGTCTGGTAC-3' (SEQ ID NO: 1057)

5'-GACUUCUUCUAUGUUUUCUGUUt-3' (SEQ ID NO: 346)
3'-AUCUGAAGGAAGAUACAAAAGACAAAG-5' (SEQ ID NO: 702)
EGFR-m4619 Target: 5'-TAGACTTCCTTCTATGTTTTCTGTTTC-3' (SEQ ID NO: 1058)

5'-UCUAUGUUUUCUGUUUCAUUGUUt-3' (SEQ ID NO: 347)
3'-GAAGAUACAAAAGACAAAGUAAACAAA-5' (SEQ ID NO: 703)
EGFR-m4627 Target: 5'-CTTCTATGTTTTCTGTTTCATTGTTTT-3' (SEQ ID NO: 1059)

5'-UGUUUUUCUCCUGGUAAACUGCag-3' (SEQ ID NO: 348)
3'-AUACAAAAAGAAGGACCAUUGACGUC-5' (SEQ ID NO: 704)

EGFR-m5006 Target: 5'-TATGTTTTTCTTCCTGGTAAACTGCAG-3' (SEQ ID NO: 1060)

5'-GUUUUUCUCCUGGUAAACUGCAGc-3' (SEQ ID NO: 349)

3'-UACAAAAAGAAGGACCAUUUGACGUCG-5' (SEQ ID NO: 705)

EGFR-m5007 Target: 5'-ATGTTTTTCTTCCTGGTAAACTGCAGC-3' (SEQ ID NO: 1061)

5'-UUUUUUCUCCUGGUAAACUGCAGcc-3' (SEQ ID NO: 350)

3'-ACAAAAAAGAAGGACCAUUUGACGUCGG-5' (SEQ ID NO: 706)

EGFR-m5008 Target: 5'-TGTTTTTCTTCCTGGTAAACTGCAGCC-3' (SEQ ID NO: 1062)

5'-UCUUCUGGUAAACUGCAGCCAAac-3' (SEQ ID NO: 351)

3'-AAAGGAAGGACCAUUUGACGUCGGUUUG-5' (SEQ ID NO: 707)

EGFR-m5012 Target: 5'-TTTCTTCCTGGTAAACTGCAGCCAAAC-3' (SEQ ID NO: 1063)

5'-CGAUCUCCUAAUGCUGUGACCCtt-3' (SEQ ID NO: 352)

3'-AAGCUAGAAGGAUUACGACACUGGGAA-5' (SEQ ID NO: 708)

EGFR-m5329 Target: 5'-TTCGATCTTCCTAATGCTGTGACCCTT-3' (SEQ ID NO: 1064)

5'-GAUCUCCUAAUGCUGUGACCCUtt-3' (SEQ ID NO: 353)

3'-AGCUAGAAGGAUUACGACACUGGGAAA-5' (SEQ ID NO: 709)

EGFR-m5330 Target: 5'-TCGATCTTCCTAATGCTGTGACCCTTT-3' (SEQ ID NO: 1065)

5'-GUUGCUACUUAACUGUAAAUtt-3' (SEQ ID NO: 354)

3'-AACAACGAUGAAGUAUUGACAUUUAAA-5' (SEQ ID NO: 710)

EGFR-m5403 Target: 5'-TTGTTGCTACTTCATAACTGTAAATTT-3' (SEQ ID NO: 1066)

5'-UUGCAGCAUCCUCUGGUUCCUAac-3' (SEQ ID NO: 355)

3'-CGAACGUCGUAGGAGACCAAAGGAUUG-5' (SEQ ID NO: 711)

EGFR-m5638 Target: 5'-GCTTGACGATCCTCTGGTTTCCTAAC-3' (SEQ ID NO: 1067)

5'-UUGCAAGCCACUCUAACUGUAGCaa-3' (SEQ ID NO: 356)

3'-GCAACGUUCGGUGAGAUUGACAUCGUU-5' (SEQ ID NO: 712)

EGFR-m5895 Target: 5'-CGTTGCAAGCCACTCTAACTGTAGCAA-3' (SEQ ID NO: 1068)

Table 5: Selected Mouse Anti-EGFR DsiRNAs, Unmodified Duplexes (Asymmetrics)

5'-GCGCAACGCGCAGCAGCCUCCUCC-3' (SEQ ID NO: 1329)

3'-GUCGCGUUGCGGUCGUCGGAGGGAGG-5' (SEQ ID NO: 617)

EGFR-m71 Target: 5'-CAGCGCAACGCGCAGCAGCCTCCCTCC-3' (SEQ ID NO: 973)

5'-GCGCAGCAGCCUCCUCCUUCUUCU-3' (SEQ ID NO: 1330)

3'-UGCGCGUCGUCGGAGGGAGGAGAAGAA-5' (SEQ ID NO: 618)

EGFR-m78 Target: 5'-ACGCGCAGCAGCCTCCCTCCTCTTCTT-3' (SEQ ID NO: 974)

5'-CCUCCUCCUUCUUCUUCUCCGCACUG-3' (SEQ ID NO: 1331)

3'-UCGGAGGGAGGAGAAGAAGGGCGUGAC-5' (SEQ ID NO: 619)

EGFR-m87 Target: 5'-AGCCTCCCTCCTCTTCTTCCCGCACTG-3' (SEQ ID NO: 975)

5'-CCCUCCUCUUCUCCCCGCACUGUGC-3' (SEQ ID NO: 1332)
3'-GAGGGAGGAGAAGAAGGGCGUGACACG-5' (SEQ ID NO: 620)

EGFR-m90 Target: 5'-CTCCCTCCTCTTCTTCCCGCACTGTGC-3' (SEQ ID NO: 976)

5'-CUCCUCUUCUCCCCGCACUGUGCGC-3' (SEQ ID NO: 1333)
3'-GGGAGGAGAAGAAGGGCGUGACACGCG-5' (SEQ ID NO: 621)

EGFR-m92 Target: 5'-CCCTCCTCTTCTTCCCGCACTGTGCGC-3' (SEQ ID NO: 977)

5'-CCUCUUCUCCCCGCACUGUGCGCUC-3' (SEQ ID NO: 1334)
3'-GAGGAGAAGAAGGGCGUGACACGCGAG-5' (SEQ ID NO: 622)

EGFR-m94 Target: 5'-CTCCTCTTCTTCCCGCACTGTGCGCTC-3' (SEQ ID NO: 978)

5'-CUUCUCCCCGCACUGUGCGCUCCUC-3' (SEQ ID NO: 1335)
3'-GAGAAGAAGGGCGUGACACGCGAGGAG-5' (SEQ ID NO: 623)

EGFR-m97 Target: 5'-CTCTTCTTCCCGCACTGTGCGCTCCTC-3' (SEQ ID NO: 979)

5'-UCUCCCCGCACUGUGCGCUCCUCCU-3' (SEQ ID NO: 1336)
3'-GAAGAAGGGCGUGACACGCGAGGAGGA-5' (SEQ ID NO: 624)

EGFR-m99 Target: 5'-CTTCTTCCCGCACTGTGCGCTCCTCCT-3' (SEQ ID NO: 980)

5'-CUUCCCCGCACUGUGCGCUCCUCCUG-3' (SEQ ID NO: 1337)
3'-AAGAAGGGCGUGACACGCGAGGAGGAC-5' (SEQ ID NO: 625)

EGFR-m100 Target: 5'-TTCTTCCCGCACTGTGCGCTCCTCCTG-3' (SEQ ID NO: 981)

5'-UUCCCCGCACUGUGCGCUCCUCCUGG-3' (SEQ ID NO: 1338)
3'-AGAAGGGCGUGACACGCGAGGAGGACC-5' (SEQ ID NO: 626)

EGFR-m101 Target: 5'-TCTTCCCGCACTGTGCGCTCCTCCTGG-3' (SEQ ID NO: 982)

5'-GUGCGCUCCUCCUGGGCUAGGGCGU-3' (SEQ ID NO: 1339)
3'-GACACGCGAGGAGGACCCGAUCCCGCA-5' (SEQ ID NO: 627)

EGFR-m111 Target: 5'-CTGTGCGCTCCTCCTGGGCTAGGGCGT-3' (SEQ ID NO: 983)

5'-CGCUCCUCCUGGGCUAGGGCGUCUG-3' (SEQ ID NO: 1340)
3'-ACGCGAGGAGGACCCGAUCCCGCAGAC-5' (SEQ ID NO: 628)

EGFR-m114 Target: 5'-TGCGCTCCTCCTGGGCTAGGGCGTCTG-3' (SEQ ID NO: 984)

5'-CACUGCUGGUGUUGCUGACCGCGCU-3' (SEQ ID NO: 1341)
3'-GUGUGACGACCACAACGACUGGCGCGA-5' (SEQ ID NO: 629)

EGFR-m333 Target: 5'-CACACTGCTGGTGTGCTGACCGCGCT-3' (SEQ ID NO: 985)

5'-ACUGCUGGUGUUGCUGACCGCGCUC-3' (SEQ ID NO: 1342)
3'-UGUGACGACCACAACGACUGGCGCGAG-5' (SEQ ID NO: 630)

EGFR-m334 Target: 5'-ACACTGCTGGTGTGCTGACCGCGCTC-3' (SEQ ID NO: 986)

5'-CUGCUGGUGUUGCUGACCGCGCUCU-3' (SEQ ID NO: 1343)

3'-GUGACGACCACAACGACUGGCGCGAGA-5' (SEQ ID NO: 631)
EGFR-m335 Target: 5'-CACTGCTGGTGTGCTGACCGCGCTCT-3' (SEQ ID NO: 987)

5'-UGCUGGUGUUGCUGACCGCGCUCUG-3' (SEQ ID NO: 1344)
3'-UGACGACCACAACGACUGGCGCGAGAC-5' (SEQ ID NO: 632)
EGFR-m336 Target: 5'-ACTGCTGGTGTGCTGACCGCGCTCTG-3' (SEQ ID NO: 988)

5'-GCUGGUGUUGCUGACCGCGCUCUGC-3' (SEQ ID NO: 1345)
3'-GACGACCACAACGACUGGCGCGAGACG-5' (SEQ ID NO: 633)
EGFR-m337 Target: 5'-CTGCTGGTGTGCTGACCGCGCTCTGC-3' (SEQ ID NO: 989)

5'-CUGGUGUUGCUGACCGCGCUCUGCG-3' (SEQ ID NO: 1346)
3'-ACGACCACAACGACUGGCGCGAGACGC-5' (SEQ ID NO: 634)
EGFR-m338 Target: 5'-TGCTGGTGTGCTGACCGCGCTCTGCG-3' (SEQ ID NO: 990)

5'-UGGUGUUGCUGACCGCGCUCUGCGC-3' (SEQ ID NO: 1347)
3'-CGACCACAACGACUGGCGCGAGACGCG-5' (SEQ ID NO: 635)
EGFR-m339 Target: 5'-GCTGGTGTGCTGACCGCGCTCTGCGC-3' (SEQ ID NO: 991)

5'-GUGUUGCUGACCGCGCUCUGCGCCG-3' (SEQ ID NO: 1348)
3'-ACCACAACGACUGGCGCGAGACGCGGC-5' (SEQ ID NO: 636)
EGFR-m341 Target: 5'-TGGTGTGCTGACCGCGCTCTGCGCCG-3' (SEQ ID NO: 992)

5'-UGUUGCUGACCGCGCUCUGCGCCGC-3' (SEQ ID NO: 1349)
3'-CCACAACGACUGGCGCGAGACGCGGCG-5' (SEQ ID NO: 637)
EGFR-m342 Target: 5'-GGTGTGCTGACCGCGCTCTGCGCCGC-3' (SEQ ID NO: 993)

5'-GUUGCUGACCGCGCUCUGCGCCGCA-3' (SEQ ID NO: 1350)
3'-CACAACGACUGGCGCGAGACGCGGCGU-5' (SEQ ID NO: 638)
EGFR-m343 Target: 5'-GTGTTGCTGACCGCGCTCTGCGCCGCA-3' (SEQ ID NO: 994)

5'-UUGCUGACCGCGCUCUGCGCCGCAG-3' (SEQ ID NO: 1351)
3'-ACAACGACUGGCGCGAGACGCGGCGUC-5' (SEQ ID NO: 639)
EGFR-m344 Target: 5'-TGTTGCTGACCGCGCTCTGCGCCGCAG-3' (SEQ ID NO: 995)

5'-CUGACCGCGCUCUGCGCCGCAGGUG-3' (SEQ ID NO: 1352)
3'-ACGACUGGCGCGAGACGCGGCGUCCAC-5' (SEQ ID NO: 640)
EGFR-m347 Target: 5'-TGCTGACCGCGCTCTGCGCCGCAGGTG-3' (SEQ ID NO: 996)

5'-UGACCGCGCUCUGCGCCGCAGGUGG-3' (SEQ ID NO: 1353)
3'-CGACUGGCGCGAGACGCGGCGUCCACC-5' (SEQ ID NO: 641)
EGFR-m348 Target: 5'-GCTGACCGCGCTCTGCGCCGCAGGTGG-3' (SEQ ID NO: 997)

5'-CUGAUUGGUGCUGUGCGAUUCAGCA-3' (SEQ ID NO: 1354)
3'-AGGACUAACCACGACACGCUAAGUCGU-5' (SEQ ID NO: 642)
EGFR-m734 Target: 5'-TCCTGATTGGTGTGCTGTGCGATTGAGCA-3' (SEQ ID NO: 998)

5'-UGAUUGGUGCUGUGCGAUUCAGCAA-3' (SEQ ID NO: 1355)
3'-GGACUAACCACGACACGCUAAGUCGUU-5' (SEQ ID NO: 643)
EGFR-m735 Target: 5'-CCTGATTGGTGCTGTGCGATTGAGCAA-3' (SEQ ID NO: 999)

5'-GAUUGGUGCUGUGCGAUUCAGCAAC-3' (SEQ ID NO: 1356)
3'-GACUAACCACGACACGCUAAGUCGUUG-5' (SEQ ID NO: 644)
EGFR-m736 Target: 5'-CTGATTGGTGCTGTGCGATTGAGCAAC-3' (SEQ ID NO: 1000)

5'-UUGGUGCUGUGCGAUUCAGCAACAA-3' (SEQ ID NO: 1357)
3'-CUAACCACGACACGCUAAGUCGUUGUU-5' (SEQ ID NO: 645)
EGFR-m738 Target: 5'-GATTGGTGCTGTGCGATTGAGCAACAA-3' (SEQ ID NO: 1001)

5'-GGUGCUGUGCGAUUCAGCAACAACC-3' (SEQ ID NO: 1358)
3'-AACCACGACACGCUAAGUCGUUGUUGG-5' (SEQ ID NO: 646)
EGFR-m740 Target: 5'-TTGGTGCTGTGCGATTGAGCAACAACC-3' (SEQ ID NO: 1002)

5'-GUGCUGUGCGAUUCAGCAACAACCC-3' (SEQ ID NO: 1359)
3'-ACCACGACACGCUAAGUCGUUGUUGGG-5' (SEQ ID NO: 647)
EGFR-m741 Target: 5'-TGGTGCTGTGCGATTGAGCAACAACCC-3' (SEQ ID NO: 1003)

5'-CAAGCUGUCCCAAUGGAAGCUGCUG-3' (SEQ ID NO: 1360)
3'-AGGUUCGACAGGGUUACCUUCGACGAC-5' (SEQ ID NO: 648)
EGFR-m879 Target: 5'-TCCAAGCTGTCCCAATGGAAGCTGCTG-3' (SEQ ID NO: 1004)

5'-GUGCCCAGCAAUGUUCCTCAUCGCUG-3' (SEQ ID NO: 1361)
3'-GACACGGGUCGUUACAAGGGUAGCGAC-5' (SEQ ID NO: 649)
EGFR-m948 Target: 5'-CTGTGCCCAGCAATGTTCCCATCGCTG-3' (SEQ ID NO: 1005)

5'-AAGUACAGCUUUGGUGCCACCUGUG-3' (SEQ ID NO: 1362)
3'-CCUUAUGUCGAAACCACGGUGGACAC-5' (SEQ ID NO: 650)
EGFR-m1154 Target: 5'-GGAAGTACAGCTTTGGTGCCACCTGTG-3' (SEQ ID NO: 1006)

5'-GUCGCAAAGUUUGUAAUGGCAUAGG-3' (SEQ ID NO: 1363)
3'-GACAGCGUUUCAAACAUUACCGUAUCC-5' (SEQ ID NO: 651)
EGFR-m1302 Target: 5'-CTGTCGCAAAGTTTGTAATGGCATAGG-3' (SEQ ID NO: 1007)

5'-GAUUCUUUCACGCGCACUCCUCCUC-3' (SEQ ID NO: 1364)
3'-CCCUAAGAAAGUGCGCGUGAGGAGAG-5' (SEQ ID NO: 652)
EGFR-m1439 Target: 5'-GGGATTCTTTACGCGCACTCCTCCTC-3' (SEQ ID NO: 1008)

5'-CAGGCUUUUUGCUGAUUCAGGCUUG-3' (SEQ ID NO: 1365)
3'-UUGUCCGAAAAACGACUAAGUCCGAAC-5' (SEQ ID NO: 653)
EGFR-m1509 Target: 5'-AACAGGCTTTTGTGCTGATTGAGGCTTG-3' (SEQ ID NO: 1009)

5'-CAGGCUUGGCCUGAUAAACUGGACUG-3' (SEQ ID NO: 1366)
3'-AAGUCCGAACCGGACUAUUGACCUGAC-5' (SEQ ID NO: 654)
EGFR-m1526 Target: 5'-TTCAGGCTTGGCCTGATAACTGGACTG-3' (SEQ ID NO: 1010)

5'-GGCUUGGCCUGAUAAACUGGACUGAC-3' (SEQ ID NO: 1367)
3'-GUCCGAACCGGACUAUUGACCUGACUG-5' (SEQ ID NO: 655)
EGFR-m1528 Target: 5'-CAGGCTTGGCCTGATAACTGGACTGAC-3' (SEQ ID NO: 1011)

5'-UUGGCCUGAUAAACUGGACUGACCUC-3' (SEQ ID NO: 1368)
3'-CGAACCGGACUAUUGACCUGACUGGAG-5' (SEQ ID NO: 656)
EGFR-m1531 Target: 5'-GCTTGGCCTGATAACTGGACTGACCTC-3' (SEQ ID NO: 1012)

5'-GCCAACUGUACCUAUGGAUGUGCUG-3' (SEQ ID NO: 1369)
3'-UGCGGUUGACAUGGAUACCUACACGAC-5' (SEQ ID NO: 657)
EGFR-m2168 Target: 5'-ACGCCAACTGTACCTATGGATGTGCTG-3' (SEQ ID NO: 1013)

5'-CUGGGAUUGUGGGUGGCCUCCUCUU-3' (SEQ ID NO: 1370)
3'-GUGACCCUAACACCCACCGGAGGAGAA-5' (SEQ ID NO: 658)
EGFR-m2253 Target: 5'-CACTGGGATTGTGGGTGGCCTCCTCTT-3' (SEQ ID NO: 1014)

5'-UGGUGGCCCCUUGGGAUUGGCCUAUU-3' (SEQ ID NO: 1371)
3'-CCACCACCGGGAACCCUAACCGGAUAA-5' (SEQ ID NO: 659)
EGFR-m2286 Target: 5'-GGTGGTGGCCCTTGGGATTGCCTATT-3' (SEQ ID NO: 1015)

5'-UUGGCCUAUUAUGCGAAGACGUCA-3' (SEQ ID NO: 1372)
3'-CUAACCGGAUAAGUACGCUUCUGCAGU-5' (SEQ ID NO: 660)
EGFR-m2301 Target: 5'-GATTGGCCTATTTCATGCGAAGACGTCA-3' (SEQ ID NO: 1016)

5'-CCGCCUGCUUCAAGAGAGAGAGCUC-3' (SEQ ID NO: 1373)
3'-GCGGCGGACGAAGUUCUCUCUCGAG-5' (SEQ ID NO: 661)
EGFR-m2350 Target: 5'-CGCCGCCTGCTTCAAGAGAGAGAGCTC-3' (SEQ ID NO: 1017)

5'-CGCCUGCUUCAAGAGAGAGAGCUCG-3' (SEQ ID NO: 1374)
3'-CGGCGGACGAAGUUCUCUCUCGAGC-5' (SEQ ID NO: 662)
EGFR-m2351 Target: 5'-GCCGCCTGCTTCAAGAGAGAGAGCTCG-3' (SEQ ID NO: 1018)

5'-GCCUGCUUCAAGAGAGAGAGCUCGU-3' (SEQ ID NO: 1375)
3'-GGCGGACGAAGUUCUCUCUCGAGCA-5' (SEQ ID NO: 663)
EGFR-m2352 Target: 5'-CCGCCTGCTTCAAGAGAGAGAGCTCGT-3' (SEQ ID NO: 1019)

5'-GGACAACCCUCAUGUAUGCCGCCUC-3' (SEQ ID NO: 1376)
3'-CACCUGUUGGGAGUACAUACGGCGGAG-5' (SEQ ID NO: 664)
EGFR-m2617 Target: 5'-GTGGACAACCCCTCATGTATGCCGCCTC-3' (SEQ ID NO: 1020)

5'-UAUGCCGCCUCCUGGGCAUCUGUCU-3' (SEQ ID NO: 1377)
3'-ACAUACGGCGGAGGACCCGUAGACAGA-5' (SEQ ID NO: 665)
EGFR-m2631 Target: 5'-TGTATGCCGCCTCCTGGGCATCTGTCT-3' (SEQ ID NO: 1021)

5'-GCUCAUGCCCUACGGUUGCCUCCUG-3' (SEQ ID NO: 1378)
3'-GUCGAGUACGGGAUGCCAACGGAGGAC-5' (SEQ ID NO: 666)

EGFR-m2683 Target: 5'-CAGCTCATGCCCTACGGTTGCCTCCTG-3' (SEQ ID NO: 1022)

5'-CUCAUGCCCUACGGUUGCCUCCUGG-3' (SEQ ID NO: 1379)

3'-UCGAGUACGGGAUGCCAACGGAGGACC-5' (SEQ ID NO: 667)

EGFR-m2684 Target: 5'-AGCTCATGCCCTACGGTTGCCTCCTGG-3' (SEQ ID NO: 1023)

5'-UCGGCGUUUGGUGCACCGUGACUUG-3' (SEQ ID NO: 1380)

3'-CUAGCCGCAAACACGUGGCACUGAAC-5' (SEQ ID NO: 668)

EGFR-m2800 Target: 5'-GATCGGCGTTTGGTGCACCGTGACTTG-3' (SEQ ID NO: 1024)

5'-GUUUGGUGCACCGUGACUUGGCAGC-3' (SEQ ID NO: 1381)

3'-CGCAAACACGUGGCACUGAACCGUCG-5' (SEQ ID NO: 669)

EGFR-m2805 Target: 5'-GCGTTTGGTGCACCGTGACTTGGCAGC-3' (SEQ ID NO: 1025)

5'-GGGCUGGCCAAACUGCUUGGUGCUG-3' (SEQ ID NO: 1382)

3'-AACCCGACCGGUUUGACGAACCACGAC-5' (SEQ ID NO: 670)

EGFR-m2879 Target: 5'-TTGGGCTGGCCAAACTGCTTGGTGCTG-3' (SEQ ID NO: 1026)

5'-GGCUGGCCAAACUGCUUGGUGCUGA-3' (SEQ ID NO: 1383)

3'-ACCCGACCGGUUUGACGAACCACGACU-5' (SEQ ID NO: 671)

EGFR-m2880 Target: 5'-TGGGCTGGCCAAACTGCTTGGTGCTGA-3' (SEQ ID NO: 1027)

5'-CUGGCCAAACUGCUUGGUGCUGAAG-3' (SEQ ID NO: 1384)

3'-CCGACCGGUUUGACGAACCACGACUUC-5' (SEQ ID NO: 672)

EGFR-m2882 Target: 5'-GGCTGGCCAAACTGCTTGGTGCTGAAG-3' (SEQ ID NO: 1028)

5'-UGGCCAAACUGCUUGGUGCUGAAGA-3' (SEQ ID NO: 1385)

3'-CGACCGGUUUGACGAACCACGACUUCU-5' (SEQ ID NO: 673)

EGFR-m2883 Target: 5'-GCTGGCCAAACTGCTTGGTGCTGAAGA-3' (SEQ ID NO: 1029)

5'-CAAGUGCUGGAUGAUAGAUGCUGAU-3' (SEQ ID NO: 1386)

3'-CAGUUCACGACCUACUAUCUACGACUA-5' (SEQ ID NO: 674)

EGFR-m3154 Target: 5'-GTCAAGTGCTGGATGATAGATGCTGAT-3' (SEQ ID NO: 1030)

5'-AAGUGCUGGAUGAUAGAUGCUGAUA-3' (SEQ ID NO: 1387)

3'-AGUUCACGACCUACUAUCUACGACUAU-5' (SEQ ID NO: 675)

EGFR-m3155 Target: 5'-TCAAGTGCTGGATGATAGATGCTGATA-3' (SEQ ID NO: 1031)

5'-AGUGCUGGAUGAUAGAUGCUGAUAG-3' (SEQ ID NO: 1388)

3'-GUUCACGACCUACUAUCUACGACUAUC-5' (SEQ ID NO: 676)

EGFR-m3156 Target: 5'-CAAGTGCTGGATGATAGATGCTGATAG-3' (SEQ ID NO: 1032)

5'-GUGCUGGAUGAUAGAUGCUGAUAGC-3' (SEQ ID NO: 1389)

3'-UUCACGACCUACUAUCUACGACUAUCG-5' (SEQ ID NO: 677)

EGFR-m3157 Target: 5'-AAGTGCTGGATGATAGATGCTGATAGC-3' (SEQ ID NO: 1033)

5'-UGCUGGAUGAUAGAUGCUGAUAGCC-3' (SEQ ID NO: 1390)

3'-UCACGACCUACUAUCUACGACUAUCGG-5' (SEQ ID NO: 678)
EGFR-m3158 Target: 5'-AGTGCTGGATGATAGATGCTGATAGCC-3' (SEQ ID NO: 1034)

5'-GCUGGAUGAUAGAUGCUGAUAGCCG-3' (SEQ ID NO: 1391)
3'-CACGACCUACUAUCUACGACUAUCGGC-5' (SEQ ID NO: 679)
EGFR-m3159 Target: 5'-GTGCTGGATGATAGATGCTGATAGCCG-3' (SEQ ID NO: 1035)

5'-CUGGAUGAUAGAUGCUGAUAGCCGC-3' (SEQ ID NO: 1392)
3'-ACGACCUACUAUCUACGACUAUCGGCG-5' (SEQ ID NO: 680)
EGFR-m3160 Target: 5'-TGCTGGATGATAGATGCTGATAGCCGC-3' (SEQ ID NO: 1036)

5'-UGGAUGAUAGAUGCUGAUAGCCGCC-3' (SEQ ID NO: 1393)
3'-CGACCUACUAUCUACGACUAUCGGCGG-5' (SEQ ID NO: 681)
EGFR-m3161 Target: 5'-GCTGGATGATAGATGCTGATAGCCGCC-3' (SEQ ID NO: 1037)

5'-GGAUGAUAGAUGCUGAUAGCCGCCC-3' (SEQ ID NO: 1394)
3'-GACCUACUAUCUACGACUAUCGGCGGG-5' (SEQ ID NO: 682)
EGFR-m3162 Target: 5'-CTGGATGATAGATGCTGATAGCCGCCC-3' (SEQ ID NO: 1038)

5'-GAUGAUAGAUGCUGAUAGCCGCCCA-3' (SEQ ID NO: 1395)
3'-ACCUACUAUCUACGACUAUCGGCGGGU-5' (SEQ ID NO: 683)
EGFR-m3163 Target: 5'-TGGATGATAGATGCTGATAGCCGCCCA-3' (SEQ ID NO: 1039)

5'-GAUAGAUGCUGAUAGCCGCCCAAAG-3' (SEQ ID NO: 1396)
3'-UACUAUCUACGACUAUCGGCGGGUUUC-5' (SEQ ID NO: 684)
EGFR-m3166 Target: 5'-ATGATAGATGCTGATAGCCGCCCAAAG-3' (SEQ ID NO: 1040)

5'-UAGAUGCUGAUAGCCGCCCAAAGUU-3' (SEQ ID NO: 1397)
3'-CUAUCUACGACUAUCGGCGGGUUCAA-5' (SEQ ID NO: 685)
EGFR-m3168 Target: 5'-GATAGATGCTGATAGCCGCCCAAAGTT-3' (SEQ ID NO: 1041)

5'-GCUGCCGUGUCAAAAGAAGACGCCU-3' (SEQ ID NO: 1398)
3'-CUCGACGGCACAGUUUCUUCUGCGGAA-5' (SEQ ID NO: 686)
EGFR-m3474 Target: 5'-GAGCTGCCGTGTCAAAGAAGACGCCTT-3' (SEQ ID NO: 1042)

5'-CUGCCGUGUCAAAAGAAGACGCCUUC-3' (SEQ ID NO: 1399)
3'-UCGACGGCACAGUUUCUUCUGCGGAAG-5' (SEQ ID NO: 687)
EGFR-m3475 Target: 5'-AGCTGCCGTGTCAAAGAAGACGCCTTC-3' (SEQ ID NO: 1043)

5'-GACGCCUUCUUGCAGCGGUACAGCU-3' (SEQ ID NO: 1400)
3'-UUCUGCGGAAGAACGUCGCCAUGUCGA-5' (SEQ ID NO: 688)
EGFR-m3491 Target: 5'-AAGACGCCTTCTTGACGCGGTACAGCT-3' (SEQ ID NO: 1044)

5'-ACGCCUUCUUGCAGCGGUACAGCUC-3' (SEQ ID NO: 1401)
3'-UCUGCGGAAGAACGUCGCCAUGUCGAG-5' (SEQ ID NO: 689)
EGFR-m3492 Target: 5'-AGACGCCTTCTTGACGCGGTACAGCTC-3' (SEQ ID NO: 1045)

5'-CGCCUUCUUGCAGCGGUACAGCUCC-3' (SEQ ID NO: 1402)
3'-CUGCGGAAGAACGUCGCCAUGUCGAGG-5' (SEQ ID NO: 690)
EGFR-m3493 Target: 5'-GACGCCTTCTTGACGCGGTACAGCTCC-3' (SEQ ID NO: 1046)

5'-GCCUUCUUGCAGCGGUACAGCUCCG-3' (SEQ ID NO: 1403)
3'-UGCGGAAGAACGUCGCCAUGUCGAGGC-5' (SEQ ID NO: 691)
EGFR-m3494 Target: 5'-ACGCCTTCTTGACGCGGTACAGCTCCG-3' (SEQ ID NO: 1047)

5'-CCUUCUUGCAGCGGUACAGCUCCGA-3' (SEQ ID NO: 1404)
3'-GCGGAAGAACGUCGCCAUGUCGAGGCU-5' (SEQ ID NO: 692)
EGFR-m3495 Target: 5'-CGCCTTCTTGACGCGGTACAGCTCCGA-3' (SEQ ID NO: 1048)

5'-CUUCUUGCAGCGGUACAGCUCCGAC-3' (SEQ ID NO: 1405)
3'-CGGAAGAACGUCGCCAUGUCGAGGCUG-5' (SEQ ID NO: 693)
EGFR-m3496 Target: 5'-GCCTTCTTGACGCGGTACAGCTCCGAC-3' (SEQ ID NO: 1049)

5'-UUCUUGCAGCGGUACAGCUCCGACC-3' (SEQ ID NO: 1406)
3'-GGAAGAACGUCGCCAUGUCGAGGCUGG-5' (SEQ ID NO: 694)
EGFR-m3497 Target: 5'-CCTTCTTGACGCGGTACAGCTCCGACC-3' (SEQ ID NO: 1050)

5'-CUGGCCUUUAAAGCAUAACUCUGAUG-3' (SEQ ID NO: 1407)
3'-CUGACCGAAAUUUCGUUUUGAGACUAC-5' (SEQ ID NO: 695)
EGFR-m4056 Target: 5'-GACTGGCTTTAAAGCATAACTCTGATG-3' (SEQ ID NO: 1051)

5'-GUGGGCCUCUCUCCUGAUGCACUUU-3' (SEQ ID NO: 1408)
3'-UUCACCCGGAGAGAGGACUACGUGAAA-5' (SEQ ID NO: 696)
EGFR-m4103 Target: 5'-AAGTGGGCCTCTCTCCTGATGCACTTT-3' (SEQ ID NO: 1052)

5'-UGGGCCUCUCUCCUGAUGCACUUUG-3' (SEQ ID NO: 1409)
3'-UCACCCGGAGAGAGGACUACGUGAAAC-5' (SEQ ID NO: 697)
EGFR-m4104 Target: 5'-AGTGGGCCTCTCTCCTGATGCACTTTG-3' (SEQ ID NO: 1053)

5'-GGGCCUCUCUCCUGAUGCACUUUGG-3' (SEQ ID NO: 1410)
3'-CACCCGGAGAGAGGACUACGUGAAACC-5' (SEQ ID NO: 698)
EGFR-m4105 Target: 5'-GTGGGCCTCTCTCCTGATGCACTTTGG-3' (SEQ ID NO: 1054)

5'-GGCCUCUCUCCUGAUGCACUUUGG-3' (SEQ ID NO: 1411)
3'-ACCCGGAGAGAGGACUACGUGAAACCC-5' (SEQ ID NO: 699)
EGFR-m4106 Target: 5'-TGGGCCTCTCTCCTGATGCACTTTGGG-3' (SEQ ID NO: 1055)

5'-CUCUCUCCUGAUGCACUUUGGGAAG-3' (SEQ ID NO: 1412)
3'-CGGAGAGAGGACUACGUGAAACCCUUC-5' (SEQ ID NO: 700)
EGFR-m4109 Target: 5'-GCCTCTCTCCTGATGCACTTTGGGAAG-3' (SEQ ID NO: 1056)

5'-UUGAUGCACUCUUGUAGUCUGGUAC-3' (SEQ ID NO: 1413)
3'-CUAACUACGUGAGAACAUCAGACCAUG-5' (SEQ ID NO: 701)
EGFR-m4309 Target: 5'-GATTGATGCACTCTTGTAGTCTGGTAC-3' (SEQ ID NO: 1057)

5'-GACUUCUUCUAUGUUUUCUGUUUC-3' (SEQ ID NO: 1414)
3'-AUCUGAAGGAAGAUACAAAAGACAAAG-5' (SEQ ID NO: 702)
EGFR-m4619 Target: 5'-TAGACTTCCTTCTATGTTTTCTGTTTC-3' (SEQ ID NO: 1058)

5'-UCUAUGUUUUCUGUUUCAUUGUUUU-3' (SEQ ID NO: 1415)
3'-GAAGAUACAAAAGACAAAGUAACAAAA-5' (SEQ ID NO: 703)
EGFR-m4627 Target: 5'-CTTCTATGTTTTCTGTTTCATTGTTTT-3' (SEQ ID NO: 1059)

5'-UGUUUUUCUCCUGGUAAACUGCAG-3' (SEQ ID NO: 1416)
3'-AUACAAAAAGAAGGACCAUUUGACGUC-5' (SEQ ID NO: 704)
EGFR-m5006 Target: 5'-TATGTTTTTCTTCTGGTAAACTGCAG-3' (SEQ ID NO: 1060)

5'-GUUUUUUCUCCUGGUAAACUGCAGC-3' (SEQ ID NO: 1417)
3'-UACAAAAAGAAGGACCAUUUGACGUCG-5' (SEQ ID NO: 705)
EGFR-m5007 Target: 5'-ATGTTTTTCTTCTGGTAAACTGCAGC-3' (SEQ ID NO: 1061)

5'-UUUUUCUCCUGGUAAACUGCAGCC-3' (SEQ ID NO: 1418)
3'-ACAAAAAGAAGGACCAUUUGACGUCGG-5' (SEQ ID NO: 706)
EGFR-m5008 Target: 5'-TGTTTTTCTTCTGGTAAACTGCAGCC-3' (SEQ ID NO: 1062)

5'-UCUCCUGGUAAACUGCAGCCAAAC-3' (SEQ ID NO: 1419)
3'-AAAGAAGGACCAUUUGACGUCGGUUUG-5' (SEQ ID NO: 707)
EGFR-m5012 Target: 5'-TTTCTTCTGGTAAACTGCAGCCAAAC-3' (SEQ ID NO: 1063)

5'-CGAUCUCCUAAUGCUGUGACCCUU-3' (SEQ ID NO: 1420)
3'-AAGCUAGAAGGAUUACGACACUGGGAA-5' (SEQ ID NO: 708)
EGFR-m5329 Target: 5'-TTCGATCTTCTAATGCTGTGACCCTT-3' (SEQ ID NO: 1064)

5'-GAUCUCCUAAUGCUGUGACCCUUU-3' (SEQ ID NO: 1421)
3'-AGCUAGAAGGAUUACGACACUGGGAAA-5' (SEQ ID NO: 709)
EGFR-m5330 Target: 5'-TCGATCTTCTAATGCTGTGACCCTTT-3' (SEQ ID NO: 1065)

5'-GUUGCUCUUAUAACUGUAAAUUU-3' (SEQ ID NO: 1422)
3'-AACAACGAUGAAGUAUUGACAUUUAAA-5' (SEQ ID NO: 710)
EGFR-m5403 Target: 5'-TTGTTGCTACTTCATAACTGTAAATTT-3' (SEQ ID NO: 1066)

5'-UUGCAGCAUCCUCUGGUUCCUAAC-3' (SEQ ID NO: 1423)
3'-CGAACGUCGUAGGAGACCAAAGGAUUG-5' (SEQ ID NO: 711)
EGFR-m5638 Target: 5'-GCTTGACGATCCTCTGGTTTCCTAAC-3' (SEQ ID NO: 1067)

5'-UUGCAAGCCACUCUAACUGUAGCAA-3' (SEQ ID NO: 1424)
3'-GCAACGUUCGGUGAGAUUGACAUCGUU-5' (SEQ ID NO: 712)
EGFR-m5895 Target: 5'-CGTTGCAAGCCACTCTAACTGTAGCAA-3' (SEQ ID NO: 1068)

Projected 21 nucleotide and component 19 nucleotide target sequences for DsiRNA of Tables 2-5 above and of Tables 7-10 below are presented in Table 6.

Table 6: DsiRNA Target Sequences (21mers) In EGFR

EGFR-31	21 nt	Target: 5'-GGCGCAGCGCGCCGCGAGCAG-3'	(SEQ ID NO: 1425)
EGFR-32	21 nt	Target: 5'-GCGCAGCGCGCCGCGAGCAGC-3'	(SEQ ID NO: 1426)
EGFR-34	21 nt	Target: 5'-GCAGCGCGCGCCGCGAGCAGCCT-3'	(SEQ ID NO: 1427)
EGFR-298	21 nt	Target: 5'-CAGCGCTCCTGGCGCTGCTGG-3'	(SEQ ID NO: 1428)
EGFR-300	21 nt	Target: 5'-GCGCTCCTGGCGCTGCTGGCT-3'	(SEQ ID NO: 1429)
EGFR-302	21 nt	Target: 5'-GCTCCTGGCGCTGCTGGCTGC-3'	(SEQ ID NO: 1430)
EGFR-390	21 nt	Target: 5'-CAGTTGGGCACCTTTTGAAGAT-3'	(SEQ ID NO: 1431)
EGFR-458	21 nt	Target: 5'-TGGGAATTTGGAAATTACCTA-3'	(SEQ ID NO: 1432)
EGFR-489	21 nt	Target: 5'-AATTATGATCTTTCCTTCTTA-3'	(SEQ ID NO: 1433)
EGFR-525	21 nt	Target: 5'-GTGGCTGGTTATGTCCTCATT-3'	(SEQ ID NO: 1434)
EGFR-676	21 nt	Target: 5'-TGCCCATGAGAAATTTACAGG-3'	(SEQ ID NO: 1435)
EGFR-701	21 nt	Target: 5'-CCTGCATGGCGCCGTGCGGTT-3'	(SEQ ID NO: 1436)
EGFR-707	21 nt	Target: 5'-TGGCGCCGTGCGGTTTCAGCAA-3'	(SEQ ID NO: 1437)
EGFR-707	21 nt	Target: 5'-TGGCGCCGTGCGGTTTCAGCAA-3'	(SEQ ID NO: 1438)
EGFR-709	21 nt	Target: 5'-GCGCCGTGCGGTTTCAGCAACA-3'	(SEQ ID NO: 1439)
EGFR-710	21 nt	Target: 5'-CGCCGTGCGGTTTCAGCAACAA-3'	(SEQ ID NO: 1440)
EGFR-827	21 nt	Target: 5'-CAGCTGCCAAAAGTGTGATCC-3'	(SEQ ID NO: 1441)
EGFR-912	21 nt	Target: 5'-ATCTGTGCCCAGCAGTGCTCC-3'	(SEQ ID NO: 1442)
EGFR-914	21 nt	Target: 5'-CTGTGCCCAGCAGTGCTCCGG-3'	(SEQ ID NO: 1443)
EGFR-926	21 nt	Target: 5'-GTGCTCCGGGCGCTGCCGTGG-3'	(SEQ ID NO: 1444)
EGFR-1005	21 nt	Target: 5'-GAGAGCGACTGCCTGGTCTGC-3'	(SEQ ID NO: 1445)
EGFR-1013	21 nt	Target: 5'-CTGCCTGGTCTGCCGCAAATT-3'	(SEQ ID NO: 1446)
EGFR-1175	21 nt	Target: 5'-GACAGATCACGGCTCGTGCGT-3'	(SEQ ID NO: 1447)
EGFR-1271	21 nt	Target: 5'-CCGCAAAAGTGTGTAACGGAAT-3'	(SEQ ID NO: 1448)
EGFR-1286	21 nt	Target: 5'-CGGAATAGGTATTGGTGAATT-3'	(SEQ ID NO: 1449)
EGFR-1330	21 nt	Target: 5'-CTACGAATATTAAACACTTCA-3'	(SEQ ID NO: 1450)
EGFR-1437	21 nt	Target: 5'-CCACAGGAAGTGGATATTCTG-3'	(SEQ ID NO: 1451)
EGFR-1475	21 nt	Target: 5'-CACAGGGTTTTTGCTGATTCA-3'	(SEQ ID NO: 1452)
EGFR-1661	21 nt	Target: 5'-TTCAGGAACAAAAATTTGTG-3'	(SEQ ID NO: 1453)
EGFR-1679	21 nt	Target: 5'-GTGCTATGCAAAATACAATAAA-3'	(SEQ ID NO: 1454)
EGFR-1723	21 nt	Target: 5'-CCGGTCAGAAAAACAAAAATTA-3'	(SEQ ID NO: 1455)
EGFR-1838	21 nt	Target: 5'-CTGCGTCTCTTGCCGGAATGT-3'	(SEQ ID NO: 1456)
EGFR-2227	21 nt	Target: 5'-GGGCCCTCCTCTTGCTGCTGG-3'	(SEQ ID NO: 1457)
EGFR-2228	21 nt	Target: 5'-GGCCCTCCTCTTGCTGCTGGT-3'	(SEQ ID NO: 1458)
EGFR-2232	21 nt	Target: 5'-CTCCTCTTGCTGCTGGTGGT-3'	(SEQ ID NO: 1459)
EGFR-2233	21 nt	Target: 5'-TCCTCTTGCTGCTGGTGGTGG-3'	(SEQ ID NO: 1460)
EGFR-2295	21 nt	Target: 5'-CGGAAGCGCACGCTGCGGAGG-3'	(SEQ ID NO: 1461)
EGFR-2298	21 nt	Target: 5'-AAGCGCACGCTGCGGAGGCTG-3'	(SEQ ID NO: 1462)
EGFR-2399	21 nt	Target: 5'-AACTGAATTCAAAAAGATCAA-3'	(SEQ ID NO: 1463)
EGFR-2417	21 nt	Target: 5'-CAAAGTGCTGGGCTCCGGTGC-3'	(SEQ ID NO: 1464)
EGFR-2419	21 nt	Target: 5'-AAGTGCTGGGCTCCGGTGCGT-3'	(SEQ ID NO: 1465)
EGFR-2420	21 nt	Target: 5'-AGTGCTGGGCTCCGGTGCGTT-3'	(SEQ ID NO: 1466)
EGFR-2421	21 nt	Target: 5'-GTGCTGGGCTCCGGTGCGTTC-3'	(SEQ ID NO: 1467)
EGFR-2422	21 nt	Target: 5'-TGCTGGGCTCCGGTGCGTTCG-3'	(SEQ ID NO: 1468)
EGFR-2591	21 nt	Target: 5'-CGTGTGCCGCTGCTGGGCAT-3'	(SEQ ID NO: 1469)
EGFR-2592	21 nt	Target: 5'-GTGTGCCGCTGCTGGGCATC-3'	(SEQ ID NO: 1470)
EGFR-2594	21 nt	Target: 5'-GTGCCGCTGCTGGGCATCTG-3'	(SEQ ID NO: 1471)
EGFR-2624	21 nt	Target: 5'-CACCGTGCACTCATCACGCA-3'	(SEQ ID NO: 1472)
EGFR-2627	21 nt	Target: 5'-CGTGCACTCATCACGCACT-3'	(SEQ ID NO: 1473)
EGFR-2631	21 nt	Target: 5'-CAGCTCATCACGCACTCATG-3'	(SEQ ID NO: 1474)

EGFR-2632 21 nt Target: 5'-AGCTCATCACGCAGCTCATGC-3' (SEQ ID NO: 1475)
EGFR-2643 21 nt Target: 5'-CAGCTCATGCCCTTCGGCTGC-3' (SEQ ID NO: 1476)
EGFR-2644 21 nt Target: 5'-AGCTCATGCCCTTCGGCTGCC-3' (SEQ ID NO: 1477)
EGFR-2754 21 nt Target: 5'-TTGGAGGACCGTCGCTTGGTG-3' (SEQ ID NO: 1478)
EGFR-2756 21 nt Target: 5'-GGAGGACCGTCGCTTGGTGCA-3' (SEQ ID NO: 1479)
EGFR-2757 21 nt Target: 5'-GAGGACCGTCGCTTGGTGAC-3' (SEQ ID NO: 1480)
EGFR-2758 21 nt Target: 5'-AGGACCGTCGCTTGGTGACAC-3' (SEQ ID NO: 1481)
EGFR-2760 21 nt Target: 5'-GACCGTCGCTTGGTGACCCGC-3' (SEQ ID NO: 1482)
EGFR-2762 21 nt Target: 5'-CCGTCGCTTGGTGACCCGCGA-3' (SEQ ID NO: 1483)
EGFR-2764 21 nt Target: 5'-GTCGCTTGGTGACCCGCGACC-3' (SEQ ID NO: 1484)
EGFR-2765 21 nt Target: 5'-TCGCTTGGTGACCCGCGACCT-3' (SEQ ID NO: 1485)
EGFR-2767 21 nt Target: 5'-GCTTGGTGACCCGCGACCTGG-3' (SEQ ID NO: 1486)
EGFR-2915 21 nt Target: 5'-GGCATTGGAATCAATTTTACA-3' (SEQ ID NO: 1487)
EGFR-3115 21 nt Target: 5'-TCAAGTGCTGGATGATAGACG-3' (SEQ ID NO: 1488)
EGFR-3117 21 nt Target: 5'-AAGTGCTGGATGATAGACGCA-3' (SEQ ID NO: 1489)
EGFR-3118 21 nt Target: 5'-AGTGCTGGATGATAGACGCAG-3' (SEQ ID NO: 1490)
EGFR-3120 21 nt Target: 5'-TGCTGGATGATAGACGCAGAT-3' (SEQ ID NO: 1491)
EGFR-3372 21 nt Target: 5'-CTCCTGAGCTCTCTGAGTGCA-3' (SEQ ID NO: 1492)
EGFR-3375 21 nt Target: 5'-CTGAGCTCTCTGAGTGCAACC-3' (SEQ ID NO: 1493)
EGFR-3440 21 nt Target: 5'-AAGCTGTCCCATCAAGGAAGA-3' (SEQ ID NO: 1494)
EGFR-3441 21 nt Target: 5'-AGCTGTCCCATCAAGGAAGAC-3' (SEQ ID NO: 1495)
EGFR-3457 21 nt Target: 5'-AAGACAGCTTCTTGACGCGAT-3' (SEQ ID NO: 1496)
EGFR-3458 21 nt Target: 5'-AGACAGCTTCTTGACGCGATA-3' (SEQ ID NO: 1497)
EGFR-3459 21 nt Target: 5'-GACAGCTTCTTGACGCGATAC-3' (SEQ ID NO: 1498)
EGFR-3460 21 nt Target: 5'-ACAGCTTCTTGACGCGATACA-3' (SEQ ID NO: 1499)
EGFR-3461 21 nt Target: 5'-CAGCTTCTTGACGCGATACAG-3' (SEQ ID NO: 1500)
EGFR-3463 21 nt Target: 5'-GCTTCTTGACGCGATACAGCT-3' (SEQ ID NO: 1501)
EGFR-3876 21 nt Target: 5'-CCACAAAGCAGTGAATTTATT-3' (SEQ ID NO: 1502)
EGFR-4178 21 nt Target: 5'-GTATATTTGAAAAAAAAAAAA-3' (SEQ ID NO: 1503)
EGFR-4205 21 nt Target: 5'-TGTGAGGATTTTATTGATTG-3' (SEQ ID NO: 1504)
EGFR-4249 21 nt Target: 5'-CGCTATTGATTTTACTTCAA-3' (SEQ ID NO: 1505)
EGFR-4284 21 nt Target: 5'-AAGGAAGAAGCTTGCTGGTAG-3' (SEQ ID NO: 1506)
EGFR-4285 21 nt Target: 5'-AGGAAGAAGCTTGCTGGTAGC-3' (SEQ ID NO: 1507)
EGFR-4286 21 nt Target: 5'-GGAAGAAGCTTGCTGGTAGCA-3' (SEQ ID NO: 1508)
EGFR-4287 21 nt Target: 5'-GAAGAAGCTTGCTGGTAGCAC-3' (SEQ ID NO: 1509)
EGFR-4288 21 nt Target: 5'-AAGAAGCTTGCTGGTAGCACT-3' (SEQ ID NO: 1510)
EGFR-4290 21 nt Target: 5'-GAAGCTTGCTGGTAGCACTTG-3' (SEQ ID NO: 1511)
EGFR-4291 21 nt Target: 5'-AAGCTTGCTGGTAGCACTTGC-3' (SEQ ID NO: 1512)
EGFR-4292 21 nt Target: 5'-AGCTTGCTGGTAGCACTTGCT-3' (SEQ ID NO: 1513)
EGFR-4293 21 nt Target: 5'-GCTTGCTGGTAGCACTTGCTA-3' (SEQ ID NO: 1514)
EGFR-4294 21 nt Target: 5'-CTTGCTGGTAGCACTTGCTAC-3' (SEQ ID NO: 1515)
EGFR-4295 21 nt Target: 5'-TTGCTGGTAGCACTTGCTACC-3' (SEQ ID NO: 1516)
EGFR-4372 21 nt Target: 5'-GGATGCTTGATTCCAGTGGTT-3' (SEQ ID NO: 1517)
EGFR-4373 21 nt Target: 5'-GATGCTTGATTCCAGTGGTTC-3' (SEQ ID NO: 1518)
EGFR-4450 21 nt Target: 5'-AGCAGGCCGGATCGGTACTGT-3' (SEQ ID NO: 1519)
EGFR-4455 21 nt Target: 5'-GCCGGATCGGTACTGTATCAA-3' (SEQ ID NO: 1520)
EGFR-4550 21 nt Target: 5'-TCCTTAGACTTACTTTTGTAA-3' (SEQ ID NO: 1521)
EGFR-4684 21 nt Target: 5'-CTGTCTTGCTGTCATGAAATC-3' (SEQ ID NO: 1522)
EGFR-4804 21 nt Target: 5'-CCTAAGGATAGCACCGCTTTT-3' (SEQ ID NO: 1523)
EGFR-4806 21 nt Target: 5'-TAAGGATAGCACCGCTTTTGT-3' (SEQ ID NO: 1524)
EGFR-4807 21 nt Target: 5'-AAGGATAGCACCGCTTTTGTT-3' (SEQ ID NO: 1525)
EGFR-4808 21 nt Target: 5'-AGGATAGCACCGCTTTTGTTT-3' (SEQ ID NO: 1526)
EGFR-4809 21 nt Target: 5'-GGATAGCACCGCTTTTGTTCT-3' (SEQ ID NO: 1527)
EGFR-4810 21 nt Target: 5'-GATAGCACCGCTTTTGTTCTC-3' (SEQ ID NO: 1528)
EGFR-4811 21 nt Target: 5'-ATAGCACCGCTTTTGTTCTCG-3' (SEQ ID NO: 1529)
EGFR-4812 21 nt Target: 5'-TAGCACCGCTTTTGTTCTCGC-3' (SEQ ID NO: 1530)
EGFR-4813 21 nt Target: 5'-AGCACCGCTTTTGTTCTCGCA-3' (SEQ ID NO: 1531)
EGFR-4816 21 nt Target: 5'-ACCGCTTTTGTTCTCGCAAAA-3' (SEQ ID NO: 1532)
EGFR-4817 21 nt Target: 5'-CCGCTTTTGTTCTCGCAAAAA-3' (SEQ ID NO: 1533)

EGFR-4818 21 nt Target: 5'-CGCTTTTGTTCCTCGCAAAAAC-3' (SEQ ID NO: 1534)
EGFR-4819 21 nt Target: 5'-GCTTTTGTTCCTCGCAAAAACG-3' (SEQ ID NO: 1535)
EGFR-4824 21 nt Target: 5'-TGTTCTCGCAAAAACGTATCT-3' (SEQ ID NO: 1536)
EGFR-4953 21 nt Target: 5'-CAAAATTAGTTTGTGTTACTT-3' (SEQ ID NO: 1537)
EGFR-4970 21 nt Target: 5'-ACTTATGGAAGATAGTTTCT-3' (SEQ ID NO: 1538)
EGFR-5003 21 nt Target: 5'-CTTCAAAAAGCTTTTTACTCAA-3' (SEQ ID NO: 1539)
EGFR-5206 21 nt Target: 5'-AAACTAGGGTTTGAAATTGAT-3' (SEQ ID NO: 1540)
EGFR-5275 21 nt Target: 5'-CCTAAAAATAATTTCTCTACAA-3' (SEQ ID NO: 1541)
EGFR-5374 21 nt Target: 5'-AACAGCAGTCCCTTTGTAAACA-3' (SEQ ID NO: 1542)
EGFR-5429 21 nt Target: 5'-TCCAATTTATCAAGGAAGAAA-3' (SEQ ID NO: 1543)
EGFR-5497 21 nt Target: 5'-CATACAAAATGTTCCTTTTGC-3' (SEQ ID NO: 1544)
EGFR-5505 21 nt Target: 5'-ATGTTCCTTTTGCTTTTAAAG-3' (SEQ ID NO: 1545)
EGFR-5506 21 nt Target: 5'-TGTTCCTTTTGCTTTTAAAGT-3' (SEQ ID NO: 1546)
EGFR-5512 21 nt Target: 5'-TTTTGCTTTTAAAGTAATTT-3' (SEQ ID NO: 1547)
EGFR-5565 21 nt Target: 5'-TTGTAAAGAAAGTATTTGATT-3' (SEQ ID NO: 1548)
EGFR-463 21 nt Target: 5'-ATTTGGAAATTACCTATGTGC-3' (SEQ ID NO: 1549)
EGFR-464 21 nt Target: 5'-TTTGGAAATTACCTATGTGCA-3' (SEQ ID NO: 1550)
EGFR-496 21 nt Target: 5'-ATCTTTCCCTTCTTAAAGACCA-3' (SEQ ID NO: 1551)
EGFR-497 21 nt Target: 5'-TCTTTCCTTCTTAAAGACCAT-3' (SEQ ID NO: 1552)
EGFR-498 21 nt Target: 5'-CTTTCCTTCTTAAAGACCATC-3' (SEQ ID NO: 1553)
EGFR-499 21 nt Target: 5'-TTTCCTTCTTAAAGACCATCC-3' (SEQ ID NO: 1554)
EGFR-500 21 nt Target: 5'-TTCCCTTCTTAAAGACCATCCA-3' (SEQ ID NO: 1555)
EGFR-501 21 nt Target: 5'-TCCTTCTTAAAGACCATCCAG-3' (SEQ ID NO: 1556)
EGFR-502 21 nt Target: 5'-CCTTCTTAAAGACCATCCAGG-3' (SEQ ID NO: 1557)
EGFR-503 21 nt Target: 5'-CTTCTTAAAGACCATCCAGGA-3' (SEQ ID NO: 1558)
EGFR-504 21 nt Target: 5'-TTCTTAAAGACCATCCAGGAG-3' (SEQ ID NO: 1559)
EGFR-505 21 nt Target: 5'-TCTTAAAGACCATCCAGGAGG-3' (SEQ ID NO: 1560)
EGFR-506 21 nt Target: 5'-CTTAAAGACCATCCAGGAGGT-3' (SEQ ID NO: 1561)
EGFR-507 21 nt Target: 5'-TTAAAGACCATCCAGGAGGTG-3' (SEQ ID NO: 1562)
EGFR-508 21 nt Target: 5'-TAAAGACCATCCAGGAGGTGG-3' (SEQ ID NO: 1563)
EGFR-509 21 nt Target: 5'-AAAGACCATCCAGGAGGTGGC-3' (SEQ ID NO: 1564)
EGFR-838 21 nt Target: 5'-AGTGTGATCCAAGCTGTCCCA-3' (SEQ ID NO: 1565)
EGFR-839 21 nt Target: 5'-GTGTGATCCAAGCTGTCCCAA-3' (SEQ ID NO: 1566)
EGFR-840 21 nt Target: 5'-TGTGATCCAAGCTGTCCCAAT-3' (SEQ ID NO: 1567)
EGFR-841 21 nt Target: 5'-GTGATCCAAGCTGTCCCAATG-3' (SEQ ID NO: 1568)
EGFR-842 21 nt Target: 5'-TGATCCAAGCTGTCCCAATGG-3' (SEQ ID NO: 1569)
EGFR-876 21 nt Target: 5'-GCAGGAGAGGAGAACTGCCAG-3' (SEQ ID NO: 1570)
EGFR-877 21 nt Target: 5'-CAGGAGAGGAGAACTGCCAGA-3' (SEQ ID NO: 1571)
EGFR-878 21 nt Target: 5'-AGGAGAGGAGAACTGCCAGAA-3' (SEQ ID NO: 1572)
EGFR-879 21 nt Target: 5'-GGAGAGGAGAACTGCCAGAAA-3' (SEQ ID NO: 1573)
EGFR-899 21 nt Target: 5'-ACTGACCAAAATCATCTGTGC-3' (SEQ ID NO: 1574)
EGFR-900 21 nt Target: 5'-CTGACCAAAATCATCTGTGCC-3' (SEQ ID NO: 1575)
EGFR-901 21 nt Target: 5'-TGACCAAAATCATCTGTGCCC-3' (SEQ ID NO: 1576)
EGFR-902 21 nt Target: 5'-GACCAAAATCATCTGTGCCC-3' (SEQ ID NO: 1577)
EGFR-903 21 nt Target: 5'-ACCAAAATCATCTGTGCCCAG-3' (SEQ ID NO: 1578)
EGFR-904 21 nt Target: 5'-CCAAATCATCTGTGCCCAGC-3' (SEQ ID NO: 1579)
EGFR-905 21 nt Target: 5'-CAAAATCATCTGTGCCCAGCA-3' (SEQ ID NO: 1580)
EGFR-954 21 nt Target: 5'-CCCAGTGACTGCTGCCACAAC-3' (SEQ ID NO: 1581)
EGFR-955 21 nt Target: 5'-CCAGTGACTGCTGCCACAACC-3' (SEQ ID NO: 1582)
EGFR-956 21 nt Target: 5'-CAGTGACTGCTGCCACAACCA-3' (SEQ ID NO: 1583)
EGFR-1313 21 nt Target: 5'-CTCACTCTCCATAAATGCTAC-3' (SEQ ID NO: 1584)
EGFR-1480 21 nt Target: 5'-GGTTTTTGCTGATTCAGGCTT-3' (SEQ ID NO: 1585)
EGFR-1481 21 nt Target: 5'-GTTTTTGCTGATTCAGGCTTG-3' (SEQ ID NO: 1586)
EGFR-1482 21 nt Target: 5'-TTTTTGCTGATTCAGGCTTGG-3' (SEQ ID NO: 1587)
EGFR-1483 21 nt Target: 5'-TTTTGCTGATTCAGGCTTGGC-3' (SEQ ID NO: 1588)
EGFR-1484 21 nt Target: 5'-TTTGCTGATTCAGGCTTGGCC-3' (SEQ ID NO: 1589)
EGFR-1485 21 nt Target: 5'-TTGCTGATTCAGGCTTGGCCT-3' (SEQ ID NO: 1590)
EGFR-1486 21 nt Target: 5'-TGCTGATTCAGGCTTGGCCTG-3' (SEQ ID NO: 1591)
EGFR-1487 21 nt Target: 5'-GCTGATTCAGGCTTGGCCTGA-3' (SEQ ID NO: 1592)

EGFR-1561 21 nt Target: 5'-CCAAGCAACATGGTCAGTTTT-3' (SEQ ID NO: 1593)
EGFR-1562 21 nt Target: 5'-CAAGCAACATGGTCAGTTTTTC-3' (SEQ ID NO: 1594)
EGFR-1563 21 nt Target: 5'-AAGCAACATGGTCAGTTTTCT-3' (SEQ ID NO: 1595)
EGFR-1691 21 nt Target: 5'-TACAATAAACTGGAAAAAACT-3' (SEQ ID NO: 1596)
EGFR-1963 21 nt Target: 5'-CTCAGGCCATGAACATCACCT-3' (SEQ ID NO: 1597)
EGFR-1964 21 nt Target: 5'-TCAGGCCATGAACATCACCTG-3' (SEQ ID NO: 1598)
EGFR-2008 21 nt Target: 5'-GTATCCAGTGTGCCCACTACA-3' (SEQ ID NO: 1599)
EGFR-2009 21 nt Target: 5'-TATCCAGTGTGCCCACTACAT-3' (SEQ ID NO: 1600)
EGFR-2010 21 nt Target: 5'-ATCCAGTGTGCCCACTACATT-3' (SEQ ID NO: 1601)
EGFR-2011 21 nt Target: 5'-TCCAGTGTGCCCACTACATTG-3' (SEQ ID NO: 1602)
EGFR-2012 21 nt Target: 5'-CCAGTGTGCCCACTACATTGA-3' (SEQ ID NO: 1603)
EGFR-2401 21 nt Target: 5'-CTGAATTCAAAAAGATCAAAG-3' (SEQ ID NO: 1604)
EGFR-2402 21 nt Target: 5'-TGAATTCAAAAAGATCAAAGT-3' (SEQ ID NO: 1605)
EGFR-2458 21 nt Target: 5'-GACTCTGGATCCCAGAAGGTG-3' (SEQ ID NO: 1606)
EGFR-2459 21 nt Target: 5'-ACTCTGGATCCCAGAAGGTGA-3' (SEQ ID NO: 1607)
EGFR-2460 21 nt Target: 5'-CTCTGGATCCCAGAAGGTGAG-3' (SEQ ID NO: 1608)
EGFR-2461 21 nt Target: 5'-TCTGGATCCCAGAAGGTGAGA-3' (SEQ ID NO: 1609)
EGFR-2462 21 nt Target: 5'-CTGGATCCCAGAAGGTGAGAA-3' (SEQ ID NO: 1610)
EGFR-2463 21 nt Target: 5'-TGGATCCCAGAAGGTGAGAAA-3' (SEQ ID NO: 1611)
EGFR-2464 21 nt Target: 5'-GGATCCCAGAAGGTGAGAAAAG-3' (SEQ ID NO: 1612)
EGFR-2465 21 nt Target: 5'-GATCCCAGAAGGTGAGAAAAGT-3' (SEQ ID NO: 1613)
EGFR-2815 21 nt Target: 5'-CGCAGCATGTCAAGATCACAG-3' (SEQ ID NO: 1614)
EGFR-2816 21 nt Target: 5'-GCAGCATGTCAAGATCACAGA-3' (SEQ ID NO: 1615)
EGFR-2817 21 nt Target: 5'-CAGCATGTCAAGATCACAGAT-3' (SEQ ID NO: 1616)
EGFR-2818 21 nt Target: 5'-AGCATGTCAAGATCACAGATT-3' (SEQ ID NO: 1617)
EGFR-2819 21 nt Target: 5'-GCATGTCAAGATCACAGATTT-3' (SEQ ID NO: 1618)
EGFR-2820 21 nt Target: 5'-CATGTCAAGATCACAGATTTT-3' (SEQ ID NO: 1619)
EGFR-2821 21 nt Target: 5'-ATGTCAAGATCACAGATTTTG-3' (SEQ ID NO: 1620)
EGFR-2822 21 nt Target: 5'-TGTCAAGATCACAGATTTTGG-3' (SEQ ID NO: 1621)
EGFR-2823 21 nt Target: 5'-GTCAAGATCACAGATTTTGGG-3' (SEQ ID NO: 1622)
EGFR-2824 21 nt Target: 5'-TCAAGATCACAGATTTTGGGC-3' (SEQ ID NO: 1623)
EGFR-2825 21 nt Target: 5'-CAAGATCACAGATTTTGGGCT-3' (SEQ ID NO: 1624)
EGFR-2826 21 nt Target: 5'-AAGATCACAGATTTTGGGCTG-3' (SEQ ID NO: 1625)
EGFR-2827 21 nt Target: 5'-AGATCACAGATTTTGGGCTGG-3' (SEQ ID NO: 1626)
EGFR-2828 21 nt Target: 5'-GATCACAGATTTTGGGCTGGC-3' (SEQ ID NO: 1627)
EGFR-2829 21 nt Target: 5'-ATCACAGATTTTGGGCTGGCC-3' (SEQ ID NO: 1628)
EGFR-2830 21 nt Target: 5'-TCACAGATTTTGGGCTGGCCA-3' (SEQ ID NO: 1629)
EGFR-2831 21 nt Target: 5'-CACAGATTTTGGGCTGGCCAA-3' (SEQ ID NO: 1630)
EGFR-2832 21 nt Target: 5'-ACAGATTTTGGGCTGGCCAAA-3' (SEQ ID NO: 1631)
EGFR-2833 21 nt Target: 5'-CAGATTTTGGGCTGGCCAAAC-3' (SEQ ID NO: 1632)
EGFR-2834 21 nt Target: 5'-AGATTTTGGGCTGGCCAAACT-3' (SEQ ID NO: 1633)
EGFR-2835 21 nt Target: 5'-GATTTTGGGCTGGCCAAACTG-3' (SEQ ID NO: 1634)
EGFR-2836 21 nt Target: 5'-ATTTTGGGCTGGCCAAACTGC-3' (SEQ ID NO: 1635)
EGFR-2837 21 nt Target: 5'-TTTTGGGCTGGCCAAACTGCT-3' (SEQ ID NO: 1636)
EGFR-2891 21 nt Target: 5'-AGGCAAAGTGCCTATCAAGTG-3' (SEQ ID NO: 1637)
EGFR-2892 21 nt Target: 5'-GGCAAAGTGCCTATCAAGTGG-3' (SEQ ID NO: 1638)
EGFR-2893 21 nt Target: 5'-GCAAAGTGCCTATCAAGTGGA-3' (SEQ ID NO: 1639)
EGFR-2894 21 nt Target: 5'-CAAAGTGCCTATCAAGTGGAT-3' (SEQ ID NO: 1640)
EGFR-2895 21 nt Target: 5'-AAAGTGCCTATCAAGTGGATG-3' (SEQ ID NO: 1641)
EGFR-2896 21 nt Target: 5'-AAGTGCCTATCAAGTGGATGG-3' (SEQ ID NO: 1642)
EGFR-2897 21 nt Target: 5'-AGTGCCTATCAAGTGGATGGC-3' (SEQ ID NO: 1643)
EGFR-3088 21 nt Target: 5'-GTACCATCGATGTCTACATGA-3' (SEQ ID NO: 1644)
EGFR-3089 21 nt Target: 5'-TACCATCGATGTCTACATGAT-3' (SEQ ID NO: 1645)
EGFR-3090 21 nt Target: 5'-ACCATCGATGTCTACATGATC-3' (SEQ ID NO: 1646)
EGFR-3091 21 nt Target: 5'-CCATCGATGTCTACATGATCA-3' (SEQ ID NO: 1647)
EGFR-3092 21 nt Target: 5'-CATCGATGTCTACATGATCAT-3' (SEQ ID NO: 1648)
EGFR-3093 21 nt Target: 5'-ATCGATGTCTACATGATCATG-3' (SEQ ID NO: 1649)
EGFR-3094 21 nt Target: 5'-TCGATGTCTACATGATCATGG-3' (SEQ ID NO: 1650)
EGFR-3095 21 nt Target: 5'-CGATGTCTACATGATCATGGT-3' (SEQ ID NO: 1651)

EGFR-3096 21 nt Target: 5'-GATGTCTACATGATCATGGTC-3' (SEQ ID NO: 1652)
EGFR-3097 21 nt Target: 5'-ATGTCTACATGATCATGGTCA-3' (SEQ ID NO: 1653)
EGFR-3098 21 nt Target: 5'-TGTCTACATGATCATGGTCAA-3' (SEQ ID NO: 1654)
EGFR-3099 21 nt Target: 5'-GTCTACATGATCATGGTCAAG-3' (SEQ ID NO: 1655)
EGFR-3100 21 nt Target: 5'-TCTACATGATCATGGTCAAGT-3' (SEQ ID NO: 1656)
EGFR-3101 21 nt Target: 5'-CTACATGATCATGGTCAAGTG-3' (SEQ ID NO: 1657)
EGFR-3102 21 nt Target: 5'-TACATGATCATGGTCAAGTGC-3' (SEQ ID NO: 1658)
EGFR-3103 21 nt Target: 5'-ACATGATCATGGTCAAGTGCT-3' (SEQ ID NO: 1659)
EGFR-3104 21 nt Target: 5'-CATGATCATGGTCAAGTGCTG-3' (SEQ ID NO: 1660)
EGFR-3105 21 nt Target: 5'-ATGATCATGGTCAAGTGCTGG-3' (SEQ ID NO: 1661)
EGFR-3106 21 nt Target: 5'-TGATCATGGTCAAGTGCTGGA-3' (SEQ ID NO: 1662)
EGFR-3107 21 nt Target: 5'-GATCATGGTCAAGTGCTGGAT-3' (SEQ ID NO: 1663)
EGFR-3108 21 nt Target: 5'-ATCATGGTCAAGTGCTGGATG-3' (SEQ ID NO: 1664)
EGFR-3109 21 nt Target: 5'-TCATGGTCAAGTGCTGGATGA-3' (SEQ ID NO: 1665)
EGFR-3110 21 nt Target: 5'-CATGGTCAAGTGCTGGATGAT-3' (SEQ ID NO: 1666)
EGFR-3111 21 nt Target: 5'-ATGGTCAAGTGCTGGATGATA-3' (SEQ ID NO: 1667)
EGFR-3112 21 nt Target: 5'-TGGTCAAGTGCTGGATGATAG-3' (SEQ ID NO: 1668)
EGFR-3113 21 nt Target: 5'-GGTCAAGTGCTGGATGATAGA-3' (SEQ ID NO: 1669)
EGFR-3169 21 nt Target: 5'-TCGAATTCTCCAAAATGGCCC-3' (SEQ ID NO: 1670)
EGFR-3170 21 nt Target: 5'-CGAATTCTCCAAAATGGCCCG-3' (SEQ ID NO: 1671)
EGFR-3220 21 nt Target: 5'-GGGATGAAAGAATGCATTTGC-3' (SEQ ID NO: 1672)
EGFR-3221 21 nt Target: 5'-GGATGAAAGAATGCATTTGCC-3' (SEQ ID NO: 1673)
EGFR-3222 21 nt Target: 5'-GATGAAAGAATGCATTTGCCA-3' (SEQ ID NO: 1674)
EGFR-3223 21 nt Target: 5'-ATGAAAGAATGCATTTGCCAA-3' (SEQ ID NO: 1675)
EGFR-3224 21 nt Target: 5'-TGAAAGAATGCATTTGCCAAG-3' (SEQ ID NO: 1676)
EGFR-3772 21 nt Target: 5'-TGGACAACCCTGACTACCAGC-3' (SEQ ID NO: 1677)
EGFR-3773 21 nt Target: 5'-GGACAACCCTGACTACCAGCA-3' (SEQ ID NO: 1678)
EGFR-3774 21 nt Target: 5'-GACAACCCTGACTACCAGCAG-3' (SEQ ID NO: 1679)
EGFR-3775 21 nt Target: 5'-ACAACCCTGACTACCAGCAGG-3' (SEQ ID NO: 1680)
EGFR-3776 21 nt Target: 5'-CAACCCTGACTACCAGCAGGA-3' (SEQ ID NO: 1681)
EGFR-3777 21 nt Target: 5'-AACCCTGACTACCAGCAGGAC-3' (SEQ ID NO: 1682)
EGFR-3778 21 nt Target: 5'-ACCCTGACTACCAGCAGGACT-3' (SEQ ID NO: 1683)
EGFR-3779 21 nt Target: 5'-CCCTGACTACCAGCAGGACTT-3' (SEQ ID NO: 1684)
EGFR-m71 21 nt Target: 5'-CAGCGCAACGCGCAGCAGCCT-3' (SEQ ID NO: 1685)
EGFR-m78 21 nt Target: 5'-ACGCGCAGCAGCCTCCCTCCT-3' (SEQ ID NO: 1686)
EGFR-m87 21 nt Target: 5'-AGCCTCCCTCCTCTTCTTCCC-3' (SEQ ID NO: 1687)
EGFR-m90 21 nt Target: 5'-CTCCCTCCTCTTCTTCCCGCA-3' (SEQ ID NO: 1688)
EGFR-m92 21 nt Target: 5'-CCCTCCTCTTCTTCCCGCACT-3' (SEQ ID NO: 1689)
EGFR-m94 21 nt Target: 5'-CTCCTCTTCTTCCCGCACTGT-3' (SEQ ID NO: 1690)
EGFR-m97 21 nt Target: 5'-CTCTTCTTCCCGCACTGTGCG-3' (SEQ ID NO: 1691)
EGFR-m99 21 nt Target: 5'-CTTCTTCCCGCACTGTGCGCT-3' (SEQ ID NO: 1692)
EGFR-m100 21 nt Target: 5'-TTCTTCCCGCACTGTGCGCTC-3' (SEQ ID NO: 1693)
EGFR-m101 21 nt Target: 5'-TCTTCCCGCACTGTGCGCTCC-3' (SEQ ID NO: 1694)
EGFR-m111 21 nt Target: 5'-CTGTGCGCTCCTCCTGGGCTA-3' (SEQ ID NO: 1695)
EGFR-m114 21 nt Target: 5'-TGCGCTCCTCCTGGGCTAGGG-3' (SEQ ID NO: 1696)
EGFR-m333 21 nt Target: 5'-CACACTGCTGGTGTGCTGAC-3' (SEQ ID NO: 1697)
EGFR-m334 21 nt Target: 5'-ACACTGCTGGTGTGCTGACC-3' (SEQ ID NO: 1698)
EGFR-m335 21 nt Target: 5'-CACTGCTGGTGTGCTGACCG-3' (SEQ ID NO: 1699)
EGFR-m336 21 nt Target: 5'-ACTGCTGGTGTGCTGACCGC-3' (SEQ ID NO: 1700)
EGFR-m337 21 nt Target: 5'-CTGCTGGTGTGCTGACCGCG-3' (SEQ ID NO: 1701)
EGFR-m338 21 nt Target: 5'-TGCTGGTGTGCTGACCGCGC-3' (SEQ ID NO: 1702)
EGFR-m339 21 nt Target: 5'-GCTGGTGTGCTGACCGCGCT-3' (SEQ ID NO: 1703)
EGFR-m341 21 nt Target: 5'-TGGTGTGCTGACCGCGCTCT-3' (SEQ ID NO: 1704)
EGFR-m342 21 nt Target: 5'-GGTGTGCTGACCGCGCTCTG-3' (SEQ ID NO: 1705)
EGFR-m343 21 nt Target: 5'-GTGTGCTGACCGCGCTCTGC-3' (SEQ ID NO: 1706)
EGFR-m344 21 nt Target: 5'-TGTTGCTGACCGCGCTCTGCG-3' (SEQ ID NO: 1707)
EGFR-m347 21 nt Target: 5'-TGCTGACCGCGCTCTGCGCCG-3' (SEQ ID NO: 1708)
EGFR-m348 21 nt Target: 5'-GCTGACCGCGCTCTGCGCCGC-3' (SEQ ID NO: 1709)
EGFR-m734 21 nt Target: 5'-TCCTGATTGGTGTGCTGTGCGAT-3' (SEQ ID NO: 1710)

EGFR-m735 21 nt Target: 5'-CCTGATTGGTGCTGTGCGATT-3' (SEQ ID NO: 1711)
EGFR-m736 21 nt Target: 5'-CTGATTGGTGCTGTGCGATT-3' (SEQ ID NO: 1712)
EGFR-m738 21 nt Target: 5'-GATTGGTGCTGTGCGATT-3' (SEQ ID NO: 1713)
EGFR-m740 21 nt Target: 5'-TTGGTGCTGTGCGATT-3' (SEQ ID NO: 1714)
EGFR-m741 21 nt Target: 5'-TGGTGCTGTGCGATT-3' (SEQ ID NO: 1715)
EGFR-m879 21 nt Target: 5'-TCCAAGCTGTCCCAATGGAAG-3' (SEQ ID NO: 1716)
EGFR-m948 21 nt Target: 5'-CTGTGCCAGCAATGTTCCCA-3' (SEQ ID NO: 1717)
EGFR-m1154 21 nt Target: 5'-GGAAGTACAGCTTTGGTGCCA-3' (SEQ ID NO: 1718)
EGFR-m1302 21 nt Target: 5'-CTGTCGCAAGTTTGTAAATGG-3' (SEQ ID NO: 1719)
EGFR-m1439 21 nt Target: 5'-GGGATTCTTTACGCGCACTC-3' (SEQ ID NO: 1720)
EGFR-m1509 21 nt Target: 5'-AACAGGCTTTTTGCTGATTCA-3' (SEQ ID NO: 1721)
EGFR-m1526 21 nt Target: 5'-TTCAGGCTTGGCCTGATAACT-3' (SEQ ID NO: 1722)
EGFR-m1528 21 nt Target: 5'-CAGGCTTGGCCTGATAACTGG-3' (SEQ ID NO: 1723)
EGFR-m1531 21 nt Target: 5'-GCTTGGCCTGATAACTGGACT-3' (SEQ ID NO: 1724)
EGFR-m2168 21 nt Target: 5'-ACGCCAACTGTACCTATGGAT-3' (SEQ ID NO: 1725)
EGFR-m2253 21 nt Target: 5'-CACTGGGATTGTGGGTGGCCT-3' (SEQ ID NO: 1726)
EGFR-m2286 21 nt Target: 5'-GGTGGTGGCCCTTGGGATTGG-3' (SEQ ID NO: 1727)
EGFR-m2301 21 nt Target: 5'-GATTGGCCTATTTCATGCGAAG-3' (SEQ ID NO: 1728)
EGFR-m2350 21 nt Target: 5'-CGCCGCCTGCTTCAAGAGAGA-3' (SEQ ID NO: 1729)
EGFR-m2351 21 nt Target: 5'-GCCGCCTGCTTCAAGAGAGAG-3' (SEQ ID NO: 1730)
EGFR-m2352 21 nt Target: 5'-CCGCCTGCTTCAAGAGAGAGA-3' (SEQ ID NO: 1731)
EGFR-m2617 21 nt Target: 5'-GTGACAAACCTCATGTATGC-3' (SEQ ID NO: 1732)
EGFR-m2631 21 nt Target: 5'-TGTATGCCCGCTCCTGGGCAT-3' (SEQ ID NO: 1733)
EGFR-m2683 21 nt Target: 5'-CAGCTCATGCCCTACGGTTGC-3' (SEQ ID NO: 1734)
EGFR-m2684 21 nt Target: 5'-AGCTCATGCCCTACGGTTGCC-3' (SEQ ID NO: 1735)
EGFR-m2800 21 nt Target: 5'-GATCGGCGTTTGGTGCACCGT-3' (SEQ ID NO: 1736)
EGFR-m2805 21 nt Target: 5'-GCGTTTGGTGCACCGTGA-3' (SEQ ID NO: 1737)
EGFR-m2879 21 nt Target: 5'-TTGGGCTGGCCAAACTGCTTG-3' (SEQ ID NO: 1738)
EGFR-m2880 21 nt Target: 5'-TGGGCTGGCCAAACTGCTTG-3' (SEQ ID NO: 1739)
EGFR-m2882 21 nt Target: 5'-GGCTGGCCAAACTGCTTGGT-3' (SEQ ID NO: 1740)
EGFR-m2883 21 nt Target: 5'-GCTGGCCAAACTGCTTGGT-3' (SEQ ID NO: 1741)
EGFR-m3154 21 nt Target: 5'-GTCAAGTGCTGGATGATAGAT-3' (SEQ ID NO: 1742)
EGFR-m3155 21 nt Target: 5'-TCAAGTGCTGGATGATAGAT-3' (SEQ ID NO: 1743)
EGFR-m3156 21 nt Target: 5'-CAAGTGCTGGATGATAGAT-3' (SEQ ID NO: 1744)
EGFR-m3157 21 nt Target: 5'-AAGTGCTGGATGATAGAT-3' (SEQ ID NO: 1745)
EGFR-m3158 21 nt Target: 5'-AGTGCTGGATGATAGAT-3' (SEQ ID NO: 1746)
EGFR-m3159 21 nt Target: 5'-GTGCTGGATGATAGAT-3' (SEQ ID NO: 1747)
EGFR-m3160 21 nt Target: 5'-TGCTGGATGATAGAT-3' (SEQ ID NO: 1748)
EGFR-m3161 21 nt Target: 5'-GCTGGATGATAGAT-3' (SEQ ID NO: 1749)
EGFR-m3162 21 nt Target: 5'-CTGGATGATAGAT-3' (SEQ ID NO: 1750)
EGFR-m3163 21 nt Target: 5'-TGGATGATAGAT-3' (SEQ ID NO: 1751)
EGFR-m3166 21 nt Target: 5'-ATGATAGATGCTGATAGCCGC-3' (SEQ ID NO: 1752)
EGFR-m3168 21 nt Target: 5'-GATAGATGCTGATAGCCGCC-3' (SEQ ID NO: 1753)
EGFR-m3474 21 nt Target: 5'-GAGCTGCCGTGTCAAAGAAGA-3' (SEQ ID NO: 1754)
EGFR-m3475 21 nt Target: 5'-AGCTGCCGTGTCAAAGAAGAC-3' (SEQ ID NO: 1755)
EGFR-m3491 21 nt Target: 5'-AAGACGCCTTCTTGCAGCGGT-3' (SEQ ID NO: 1756)
EGFR-m3492 21 nt Target: 5'-AGACGCCTTCTTGCAGCGGT-3' (SEQ ID NO: 1757)
EGFR-m3493 21 nt Target: 5'-GACGCCTTCTTGCAGCGGT-3' (SEQ ID NO: 1758)
EGFR-m3494 21 nt Target: 5'-ACGCCTTCTTGCAGCGGT-3' (SEQ ID NO: 1759)
EGFR-m3495 21 nt Target: 5'-CGCCTTCTTGCAGCGGT-3' (SEQ ID NO: 1760)
EGFR-m3496 21 nt Target: 5'-GCCTTCTTGCAGCGGT-3' (SEQ ID NO: 1761)
EGFR-m3497 21 nt Target: 5'-CCTTCTTGCAGCGGT-3' (SEQ ID NO: 1762)
EGFR-m4056 21 nt Target: 5'-GACTGGCTTTAAAGCATAACT-3' (SEQ ID NO: 1763)
EGFR-m4103 21 nt Target: 5'-AAGTGGGCCTCTCTCTGATG-3' (SEQ ID NO: 1764)
EGFR-m4104 21 nt Target: 5'-AGTGGGCCTCTCTCTGATG-3' (SEQ ID NO: 1765)
EGFR-m4105 21 nt Target: 5'-GTGGGCCTCTCTCTGATGCA-3' (SEQ ID NO: 1766)
EGFR-m4106 21 nt Target: 5'-TGCGCCTCTCTCTGATGCAC-3' (SEQ ID NO: 1767)
EGFR-m4109 21 nt Target: 5'-GCCCTCTCTCTGATGCACTTT-3' (SEQ ID NO: 1768)
EGFR-m4309 21 nt Target: 5'-GATTGATGCACTCTTGTAGTC-3' (SEQ ID NO: 1769)

EGFR-m4619 21 nt Target: 5'-TAGACTTCCTTCTATGTTTTTC-3' (SEQ ID NO: 1770)
 EGFR-m4627 21 nt Target: 5'-CTTCTATGTTTTCTGTTTCAT-3' (SEQ ID NO: 1771)
 EGFR-m5006 21 nt Target: 5'-TATGTTTTTCTTCTGGTAAA-3' (SEQ ID NO: 1772)
 EGFR-m5007 21 nt Target: 5'-ATGTTTTTCTTCTGGTAAAC-3' (SEQ ID NO: 1773)
 EGFR-m5008 21 nt Target: 5'-TGTTTTTCTTCTGGTAAACT-3' (SEQ ID NO: 1774)
 EGFR-m5012 21 nt Target: 5'-TTTCTTCTGGTAAACTGCAG-3' (SEQ ID NO: 1775)
 EGFR-m5329 21 nt Target: 5'-TTCGATCTTCTAATGCTGTG-3' (SEQ ID NO: 1776)
 EGFR-m5330 21 nt Target: 5'-TCGATCTTCTAATGCTGTGA-3' (SEQ ID NO: 1777)
 EGFR-m5403 21 nt Target: 5'-TTGTTGCTACTTCATAACTGT-3' (SEQ ID NO: 1778)
 EGFR-m5638 21 nt Target: 5'-GCTTGACAGCATCCTCTGGTTT-3' (SEQ ID NO: 1779)
 EGFR-m5895 21 nt Target: 5'-CGTTGCAAGCCACTCTAACTG-3' (SEQ ID NO: 1780)

21 NUCLEOTIDE TARGET mRNA SEQUENCES

EGFR-31 21 nt Target: 5'-GGCGCAGCGCGCCGAGCAG-3' (SEQ ID NO: 2509)
 EGFR-32 21 nt Target: 5'-GCGCAGCGCGCCGAGCAGC-3' (SEQ ID NO: 2510)
 EGFR-34 21 nt Target: 5'-GCAGCGCGCCGAGCAGCCU-3' (SEQ ID NO: 2511)
 EGFR-298 21 nt Target: 5'-CAGCGCUCCUGGCGUGCUGG-3' (SEQ ID NO: 2512)
 EGFR-300 21 nt Target: 5'-GCGCUCCUGGCGUGCUGGCU-3' (SEQ ID NO: 2513)
 EGFR-302 21 nt Target: 5'-GCUCCUGGCGUGCUGGCGUC-3' (SEQ ID NO: 2514)
 EGFR-390 21 nt Target: 5'-CAGUUGGGCACUUUUGAAGAU-3' (SEQ ID NO: 2515)
 EGFR-458 21 nt Target: 5'-UGGGAAUUUGGAAAUUACCUA-3' (SEQ ID NO: 2516)
 EGFR-489 21 nt Target: 5'-AAUUAUGAUCUUUCCUUCUUA-3' (SEQ ID NO: 2517)
 EGFR-525 21 nt Target: 5'-GUGGCGUGUUAUGUCCUCAUU-3' (SEQ ID NO: 2518)
 EGFR-676 21 nt Target: 5'-UGCCCAUGAGAAAUUACAGG-3' (SEQ ID NO: 2519)
 EGFR-701 21 nt Target: 5'-CCUGCAUGGCGCGGUGCGGUU-3' (SEQ ID NO: 2520)
 EGFR-707 21 nt Target: 5'-UGGCGCCGUGCGGUUCAGCAA-3' (SEQ ID NO: 2521)
 EGFR-707 21 nt Target: 5'-UGGCGCCGUGCGGUUCAGCAA-3' (SEQ ID NO: 2522)
 EGFR-709 21 nt Target: 5'-GCGCCGUGCGGUUCAGCAACA-3' (SEQ ID NO: 2523)
 EGFR-710 21 nt Target: 5'-CGCCGUGCGGUUCAGCAACAA-3' (SEQ ID NO: 2524)
 EGFR-827 21 nt Target: 5'-CAGCUGCCAAAAGUGUGAUCC-3' (SEQ ID NO: 2525)
 EGFR-912 21 nt Target: 5'-AUCUGUGCCCAGCAGUGCUCC-3' (SEQ ID NO: 2526)
 EGFR-914 21 nt Target: 5'-CUGUGCCCAGCAGUGCUCCGG-3' (SEQ ID NO: 2527)
 EGFR-926 21 nt Target: 5'-GUGCUCGCGGCGUGCCGUGG-3' (SEQ ID NO: 2528)
 EGFR-1005 21 nt Target: 5'-GAGAGCGACUGCCUGGUCUGC-3' (SEQ ID NO: 2529)
 EGFR-1013 21 nt Target: 5'-CUGCCUGGUCUGCCGCAAUU-3' (SEQ ID NO: 2530)
 EGFR-1175 21 nt Target: 5'-GACAGAUCACGGCUCGUGCGU-3' (SEQ ID NO: 2531)
 EGFR-1271 21 nt Target: 5'-CCGCAAAGUGUGUAAACGGAU-3' (SEQ ID NO: 2532)
 EGFR-1286 21 nt Target: 5'-CGGAAUAGGUUAUUGGUGAAU-3' (SEQ ID NO: 2533)
 EGFR-1330 21 nt Target: 5'-CUACGAAUAUAAACACUUCA-3' (SEQ ID NO: 2534)
 EGFR-1437 21 nt Target: 5'-CCACAGGAACUGGAUAUUCUG-3' (SEQ ID NO: 2535)
 EGFR-1475 21 nt Target: 5'-CACAGGGUUUUGCUGAUUCA-3' (SEQ ID NO: 2536)
 EGFR-1661 21 nt Target: 5'-UUCAGGAAACAAAAUUUGUG-3' (SEQ ID NO: 2537)
 EGFR-1679 21 nt Target: 5'-GUGCUAUGCAAAUACAAUAAA-3' (SEQ ID NO: 2538)
 EGFR-1723 21 nt Target: 5'-CCGGUCAGAAAACCAAAUUA-3' (SEQ ID NO: 2539)
 EGFR-1838 21 nt Target: 5'-CUGCGUCUCUUGCCGGAAGU-3' (SEQ ID NO: 2540)
 EGFR-2227 21 nt Target: 5'-GGGCCCUCUCUUGCUGCUGG-3' (SEQ ID NO: 2541)
 EGFR-2228 21 nt Target: 5'-GGCCCUCUCUUGCUGCUGGU-3' (SEQ ID NO: 2542)
 EGFR-2232 21 nt Target: 5'-CUCCUCUUGCUGCUGGUGUG-3' (SEQ ID NO: 2543)
 EGFR-2233 21 nt Target: 5'-UCCUCUUGCUGCUGGUGUGG-3' (SEQ ID NO: 2544)
 EGFR-2295 21 nt Target: 5'-CGGAAGCGCACGUGCGGAGG-3' (SEQ ID NO: 2545)
 EGFR-2298 21 nt Target: 5'-AAGCGCACGUGCGGAGGCUG-3' (SEQ ID NO: 2546)
 EGFR-2399 21 nt Target: 5'-AACUGAAUCAAAGAUCAA-3' (SEQ ID NO: 2547)
 EGFR-2417 21 nt Target: 5'-CAAAGUGCUGGGCUCCGGUGC-3' (SEQ ID NO: 2548)
 EGFR-2419 21 nt Target: 5'-AAGUGCUGGGCUCCGGUGCGU-3' (SEQ ID NO: 2549)
 EGFR-2420 21 nt Target: 5'-AGUGCUGGGCUCCGGUGCGUU-3' (SEQ ID NO: 2550)
 EGFR-2421 21 nt Target: 5'-GUGCUGGGCUCCGGUGCGUUC-3' (SEQ ID NO: 2551)
 EGFR-2422 21 nt Target: 5'-UGCUGGGCUCCGGUGCGUUCG-3' (SEQ ID NO: 2552)
 EGFR-2591 21 nt Target: 5'-CGUGUGCCGCCUGCUGGGCAU-3' (SEQ ID NO: 2553)
 EGFR-2592 21 nt Target: 5'-GUGUGCCGCCUGCUGGGCAUC-3' (SEQ ID NO: 2554)

EGFR-2594 21 nt Target: 5'-GUGCCGCCUGCUGGGCAUCUG-3' (SEQ ID NO: 2555)
 EGFR-2624 21 nt Target: 5'-CACCGUGCAGCUCAUCACGCA-3' (SEQ ID NO: 2556)
 EGFR-2627 21 nt Target: 5'-CGUGCAGCUCAUCACGCAGCU-3' (SEQ ID NO: 2557)
 EGFR-2631 21 nt Target: 5'-CAGCUCAUCACGCAGCUCAUG-3' (SEQ ID NO: 2558)
 EGFR-2632 21 nt Target: 5'-AGCUCAUCACGCAGCUCAUGC-3' (SEQ ID NO: 2559)
 EGFR-2643 21 nt Target: 5'-CAGCUCAUGCCCUUCGGCUGC-3' (SEQ ID NO: 2560)
 EGFR-2644 21 nt Target: 5'-AGCUCAUGCCCUUCGGCUGCC-3' (SEQ ID NO: 2561)
 EGFR-2754 21 nt Target: 5'-UUGGAGGACCGUCGCUUGGUG-3' (SEQ ID NO: 2562)
 EGFR-2756 21 nt Target: 5'-GGAGGACCGUCGCUUGGUGCA-3' (SEQ ID NO: 2563)
 EGFR-2757 21 nt Target: 5'-GAGGACCGUCGCUUGGUGCAC-3' (SEQ ID NO: 2564)
 EGFR-2758 21 nt Target: 5'-AGGACCGUCGCUUGGUGCACC-3' (SEQ ID NO: 2565)
 EGFR-2760 21 nt Target: 5'-GACCGUCGCUUGGUGCACC GC-3' (SEQ ID NO: 2566)
 EGFR-2762 21 nt Target: 5'-CCGUCGCUUGGUGCACC GC GA-3' (SEQ ID NO: 2567)
 EGFR-2764 21 nt Target: 5'-GUCGCUUGGUGCACC GC GACC-3' (SEQ ID NO: 2568)
 EGFR-2765 21 nt Target: 5'-UCGCUUGGUGCACC GC GACCU-3' (SEQ ID NO: 2569)
 EGFR-2767 21 nt Target: 5'-GCUUGGUGCACC GC GACCU GG-3' (SEQ ID NO: 2570)
 EGFR-2915 21 nt Target: 5'-GGCAUUGGAAUCAAUUUUACA-3' (SEQ ID NO: 2571)
 EGFR-3115 21 nt Target: 5'-UCAAGUGCUGGAUGAUAGACG-3' (SEQ ID NO: 2572)
 EGFR-3117 21 nt Target: 5'-AAGUGCUGGAUGAUAGACGCA-3' (SEQ ID NO: 2573)
 EGFR-3118 21 nt Target: 5'-AGUGCUGGAUGAUAGACGCAG-3' (SEQ ID NO: 2574)
 EGFR-3120 21 nt Target: 5'-UGCUGGAUGAUAGACGCAGAU-3' (SEQ ID NO: 2575)
 EGFR-3372 21 nt Target: 5'-CUCCUGAGCUCUCUGAGUGCA-3' (SEQ ID NO: 2576)
 EGFR-3375 21 nt Target: 5'-CUGAGCUCUCUGAGUGCAACC-3' (SEQ ID NO: 2577)
 EGFR-3440 21 nt Target: 5'-AAGCUGUCCCAUCAAGGAAGA-3' (SEQ ID NO: 2578)
 EGFR-3441 21 nt Target: 5'-AGCUGUCCCAUCAAGGAAGAC-3' (SEQ ID NO: 2579)
 EGFR-3457 21 nt Target: 5'-AAGACAGCUUCUUGCAGCGAU-3' (SEQ ID NO: 2580)
 EGFR-3458 21 nt Target: 5'-AGACAGCUUCUUGCAGCGAUA-3' (SEQ ID NO: 2581)
 EGFR-3459 21 nt Target: 5'-GACAGCUUCUUGCAGCGAUAC-3' (SEQ ID NO: 2582)
 EGFR-3460 21 nt Target: 5'-ACAGCUUCUUGCAGCGAUACA-3' (SEQ ID NO: 2583)
 EGFR-3461 21 nt Target: 5'-CAGCUUCUUGCAGCGAUACAG-3' (SEQ ID NO: 2584)
 EGFR-3463 21 nt Target: 5'-GCUUCUUGCAGCGAUACAGCU-3' (SEQ ID NO: 2585)
 EGFR-3876 21 nt Target: 5'-CCACAAAGCAGUGAAUUUAUU-3' (SEQ ID NO: 2586)
 EGFR-4178 21 nt Target: 5'-GUAUAUUUGAAAAAAAAAAAA-3' (SEQ ID NO: 2587)
 EGFR-4205 21 nt Target: 5'-UGUGAGGAUUUUUAUUGAUUG-3' (SEQ ID NO: 2588)
 EGFR-4249 21 nt Target: 5'-CGCUAUUGAUUUUUACUUCAA-3' (SEQ ID NO: 2589)
 EGFR-4284 21 nt Target: 5'-AAGGAAGAAGCUUGCUGGUAG-3' (SEQ ID NO: 2590)
 EGFR-4285 21 nt Target: 5'-AGGAAGAAGCUUGCUGGUAGC-3' (SEQ ID NO: 2591)
 EGFR-4286 21 nt Target: 5'-GGAAGAAGCUUGCUGGUAGCA-3' (SEQ ID NO: 2592)
 EGFR-4287 21 nt Target: 5'-GAAGAAGCUUGCUGGUAGCAC-3' (SEQ ID NO: 2593)
 EGFR-4288 21 nt Target: 5'-AAGAAGCUUGCUGGUAGCACU-3' (SEQ ID NO: 2594)
 EGFR-4290 21 nt Target: 5'-GAAGCUUGCUGGUAGCACUUG-3' (SEQ ID NO: 2595)
 EGFR-4291 21 nt Target: 5'-AAGCUUGCUGGUAGCACUUGC-3' (SEQ ID NO: 2596)
 EGFR-4292 21 nt Target: 5'-AGCUUGCUGGUAGCACUUGC U-3' (SEQ ID NO: 2597)
 EGFR-4293 21 nt Target: 5'-GCUUGCUGGUAGCACUUGC UA-3' (SEQ ID NO: 2598)
 EGFR-4294 21 nt Target: 5'-CUUGCUGGUAGCACUUGC UA C-3' (SEQ ID NO: 2599)
 EGFR-4295 21 nt Target: 5'-UUGCUGGUAGCACUUGC UA CC-3' (SEQ ID NO: 2600)
 EGFR-4372 21 nt Target: 5'-GGAUGCUUGAUUCCAGUGGUU-3' (SEQ ID NO: 2601)
 EGFR-4373 21 nt Target: 5'-GAUGCUUGAUUCCAGUGGUUC-3' (SEQ ID NO: 2602)
 EGFR-4450 21 nt Target: 5'-AGCAGGCCGGAUCGGUACUGU-3' (SEQ ID NO: 2603)
 EGFR-4455 21 nt Target: 5'-GCCGGAUCGGUACUGUAUCAA-3' (SEQ ID NO: 2604)
 EGFR-4550 21 nt Target: 5'-UCCUUAGACUUACUUUUGUAA-3' (SEQ ID NO: 2605)
 EGFR-4684 21 nt Target: 5'-CUGUCUUGCUGUCAUGAAAUC-3' (SEQ ID NO: 2606)
 EGFR-4804 21 nt Target: 5'-CCUAAGGAUAGCACCGCUUUU-3' (SEQ ID NO: 2607)
 EGFR-4806 21 nt Target: 5'-UAAGGAUAGCACCGCUUUUGU-3' (SEQ ID NO: 2608)
 EGFR-4807 21 nt Target: 5'-AAGGAUAGCACCGCUUUUGUU-3' (SEQ ID NO: 2609)
 EGFR-4808 21 nt Target: 5'-AGGAUAGCACCGCUUUUGUUC-3' (SEQ ID NO: 2610)
 EGFR-4809 21 nt Target: 5'-GGAUAGCACCGCUUUUGUUCU-3' (SEQ ID NO: 2611)
 EGFR-4810 21 nt Target: 5'-GAUAGCACCGCUUUUGUUCUC-3' (SEQ ID NO: 2612)
 EGFR-4811 21 nt Target: 5'-AUAGCACCGCUUUUGUUCUCG-3' (SEQ ID NO: 2613)

EGFR-4812 21 nt Target: 5'-UAGCACCGCUUUUGUUCUCGC-3' (SEQ ID NO: 2614)
EGFR-4813 21 nt Target: 5'-AGCACCGCUUUUGUUCUCGCA-3' (SEQ ID NO: 2615)
EGFR-4816 21 nt Target: 5'-ACCGCUUUUGUUCUCGCAAAA-3' (SEQ ID NO: 2616)
EGFR-4817 21 nt Target: 5'-CCGCUUUUGUUCUCGCAAAA-3' (SEQ ID NO: 2617)
EGFR-4818 21 nt Target: 5'-CGCUUUUGUUCUCGCAAAAAC-3' (SEQ ID NO: 2618)
EGFR-4819 21 nt Target: 5'-GCUUUUGUUCUCGCAAAAACG-3' (SEQ ID NO: 2619)
EGFR-4824 21 nt Target: 5'-UGUUCUCGCAAAAACGUUUCU-3' (SEQ ID NO: 2620)
EGFR-4953 21 nt Target: 5'-CAAAAUUAGUUUGUUAUUCU-3' (SEQ ID NO: 2621)
EGFR-4970 21 nt Target: 5'-ACUUAUGGAAGAUAGUUUUCU-3' (SEQ ID NO: 2622)
EGFR-5003 21 nt Target: 5'-CUUCAAAAGCUUUUACUCAA-3' (SEQ ID NO: 2623)
EGFR-5206 21 nt Target: 5'-AAACUAGGGUUUGAAAUUGAU-3' (SEQ ID NO: 2624)
EGFR-5275 21 nt Target: 5'-CCUAAAAUAAUUCUCUACAA-3' (SEQ ID NO: 2625)
EGFR-5374 21 nt Target: 5'-AACAGCAGUCCUUUGUAAACA-3' (SEQ ID NO: 2626)
EGFR-5429 21 nt Target: 5'-UCCAAUUUAUCAAGGAAGAAA-3' (SEQ ID NO: 2627)
EGFR-5497 21 nt Target: 5'-CAUACAAAUGUCCUUUUGC-3' (SEQ ID NO: 2628)
EGFR-5505 21 nt Target: 5'-AUGUCCUUUUGCUUUUAAAG-3' (SEQ ID NO: 2629)
EGFR-5506 21 nt Target: 5'-UGUCCUUUUGCUUUUAAAGU-3' (SEQ ID NO: 2630)
EGFR-5512 21 nt Target: 5'-UUUUGCUUUUAAAGUAAUUU-3' (SEQ ID NO: 2631)
EGFR-5565 21 nt Target: 5'-UGUUAAGAAAGUAUUUGAUU-3' (SEQ ID NO: 2632)
EGFR-463 21 nt Target: 5'-AUUUGGAAAUUACCUAUGUGC-3' (SEQ ID NO: 2633)
EGFR-464 21 nt Target: 5'-UUUGGAAAUUACCUAUGUGCA-3' (SEQ ID NO: 2634)
EGFR-496 21 nt Target: 5'-AUCUUCCUUCUUAAGACCA-3' (SEQ ID NO: 2635)
EGFR-497 21 nt Target: 5'-UCUUCCUUCUUAAGACCAU-3' (SEQ ID NO: 2636)
EGFR-498 21 nt Target: 5'-CUUCCUUCUUAAGACCAUC-3' (SEQ ID NO: 2637)
EGFR-499 21 nt Target: 5'-UUCCUUCUUAAGACCAUCC-3' (SEQ ID NO: 2638)
EGFR-500 21 nt Target: 5'-UCCUUCUUAAGACCAUCCA-3' (SEQ ID NO: 2639)
EGFR-501 21 nt Target: 5'-UCCUUCUUAAGACCAUCCAG-3' (SEQ ID NO: 2640)
EGFR-502 21 nt Target: 5'-CCUUCUUAAGACCAUCCAGG-3' (SEQ ID NO: 2641)
EGFR-503 21 nt Target: 5'-CUUCUUAAGACCAUCCAGGA-3' (SEQ ID NO: 2642)
EGFR-504 21 nt Target: 5'-UUCUUAAGACCAUCCAGGAG-3' (SEQ ID NO: 2643)
EGFR-505 21 nt Target: 5'-UCUUAAGACCAUCCAGGAGG-3' (SEQ ID NO: 2644)
EGFR-506 21 nt Target: 5'-CUUAAAGACCAUCCAGGAGGU-3' (SEQ ID NO: 2645)
EGFR-507 21 nt Target: 5'-UUAAGACCAUCCAGGAGGUG-3' (SEQ ID NO: 2646)
EGFR-508 21 nt Target: 5'-UAAAGACCAUCCAGGAGGUGG-3' (SEQ ID NO: 2647)
EGFR-509 21 nt Target: 5'-AAAGACCAUCCAGGAGGUGGC-3' (SEQ ID NO: 2648)
EGFR-838 21 nt Target: 5'-AGUGUGAUCCAAGCUGUCCCA-3' (SEQ ID NO: 2649)
EGFR-839 21 nt Target: 5'-GUGUGAUCCAAGCUGUCCCAA-3' (SEQ ID NO: 2650)
EGFR-840 21 nt Target: 5'-UGUGAUCCAAGCUGUCCCAAU-3' (SEQ ID NO: 2651)
EGFR-841 21 nt Target: 5'-GUGAUCCAAGCUGUCCCAAUG-3' (SEQ ID NO: 2652)
EGFR-842 21 nt Target: 5'-UGAUCCAAGCUGUCCCAAUGG-3' (SEQ ID NO: 2653)
EGFR-876 21 nt Target: 5'-GCAGGAGAGGAGAACUGCCAG-3' (SEQ ID NO: 2654)
EGFR-877 21 nt Target: 5'-CAGGAGAGGAGAACUGCCAGA-3' (SEQ ID NO: 2655)
EGFR-878 21 nt Target: 5'-AGGAGAGGAGAACUGCCAGAA-3' (SEQ ID NO: 2656)
EGFR-879 21 nt Target: 5'-GGAGAGGAGAACUGCCAGAAA-3' (SEQ ID NO: 2657)
EGFR-899 21 nt Target: 5'-ACUGACCAAAUUAUCUGUGC-3' (SEQ ID NO: 2658)
EGFR-900 21 nt Target: 5'-CUGACCAAAUUAUCUGUGCC-3' (SEQ ID NO: 2659)
EGFR-901 21 nt Target: 5'-UGACCAAAUUAUCUGUGCCC-3' (SEQ ID NO: 2660)
EGFR-902 21 nt Target: 5'-GACCAAAUUAUCUGUGCCCA-3' (SEQ ID NO: 2661)
EGFR-903 21 nt Target: 5'-ACCAAAUUAUCUGUGCCCAG-3' (SEQ ID NO: 2662)
EGFR-904 21 nt Target: 5'-CCAAAUUAUCUGUGCCCAGC-3' (SEQ ID NO: 2663)
EGFR-905 21 nt Target: 5'-CAAAAUUAUCUGUGCCCAGCA-3' (SEQ ID NO: 2664)
EGFR-954 21 nt Target: 5'-CCCAGUGACUGCUGCCACAAC-3' (SEQ ID NO: 2665)
EGFR-955 21 nt Target: 5'-CCAGUGACUGCUGCCACAACC-3' (SEQ ID NO: 2666)
EGFR-956 21 nt Target: 5'-CAGUGACUGCUGCCACAACCA-3' (SEQ ID NO: 2667)
EGFR-1313 21 nt Target: 5'-CUCACUCUCCAUAUAUGCUAC-3' (SEQ ID NO: 2668)
EGFR-1480 21 nt Target: 5'-GGUUUUUGCUGAUUCAGGCUU-3' (SEQ ID NO: 2669)
EGFR-1481 21 nt Target: 5'-GUUUUUGCUGAUUCAGGCUUG-3' (SEQ ID NO: 2670)
EGFR-1482 21 nt Target: 5'-UUUUUUGCUGAUUCAGGCUUGG-3' (SEQ ID NO: 2671)
EGFR-1483 21 nt Target: 5'-UUUUGCUGAUUCAGGCUUGGC-3' (SEQ ID NO: 2672)

EGFR-1484 21 nt Target: 5'-UUUGCUGAUUCAGGCUUGGCC-3' (SEQ ID NO: 2673)
EGFR-1485 21 nt Target: 5'-UUGCUGAUUCAGGCUUGGCCU-3' (SEQ ID NO: 2674)
EGFR-1486 21 nt Target: 5'-UGCUGAUUCAGGCUUGGCCUG-3' (SEQ ID NO: 2675)
EGFR-1487 21 nt Target: 5'-GCUGAUUCAGGCUUGGCCUGA-3' (SEQ ID NO: 2676)
EGFR-1561 21 nt Target: 5'-CCAAGCAACAUGGUCAGUUUU-3' (SEQ ID NO: 2677)
EGFR-1562 21 nt Target: 5'-CAAGCAACAUGGUCAGUUUUC-3' (SEQ ID NO: 2678)
EGFR-1563 21 nt Target: 5'-AAGCAACAUGGUCAGUUUUCU-3' (SEQ ID NO: 2679)
EGFR-1691 21 nt Target: 5'-UACAAUAAAACUGGAAAAAACU-3' (SEQ ID NO: 2680)
EGFR-1963 21 nt Target: 5'-CUCAGGCCAUGAACAUACCUC-3' (SEQ ID NO: 2681)
EGFR-1964 21 nt Target: 5'-UCAGGCCAUGAACAUACCUG-3' (SEQ ID NO: 2682)
EGFR-2008 21 nt Target: 5'-GUAUCCAGUGUGCCCACUACA-3' (SEQ ID NO: 2683)
EGFR-2009 21 nt Target: 5'-UAUCCAGUGUGCCCACUACAU-3' (SEQ ID NO: 2684)
EGFR-2010 21 nt Target: 5'-AUCCAGUGUGCCCACUACAUU-3' (SEQ ID NO: 2685)
EGFR-2011 21 nt Target: 5'-UCCAGUGUGCCCACUACAUUG-3' (SEQ ID NO: 2686)
EGFR-2012 21 nt Target: 5'-CCAGUGUGCCCACUACAUUGA-3' (SEQ ID NO: 2687)
EGFR-2401 21 nt Target: 5'-CUGAAUUCAAAAAGAUCAAAG-3' (SEQ ID NO: 2688)
EGFR-2402 21 nt Target: 5'-UGAAUUCAAAAAGAUCAAAGU-3' (SEQ ID NO: 2689)
EGFR-2458 21 nt Target: 5'-GACUCUGGAUCCCAGAAAGGUG-3' (SEQ ID NO: 2690)
EGFR-2459 21 nt Target: 5'-ACUCUGGAUCCCAGAAAGGUGA-3' (SEQ ID NO: 2691)
EGFR-2460 21 nt Target: 5'-CUCUGGAUCCCAGAAAGGUGAG-3' (SEQ ID NO: 2692)
EGFR-2461 21 nt Target: 5'-UCUGGAUCCCAGAAAGGUGAGA-3' (SEQ ID NO: 2693)
EGFR-2462 21 nt Target: 5'-CUGGAUCCCAGAAAGGUGAGAA-3' (SEQ ID NO: 2694)
EGFR-2463 21 nt Target: 5'-UGGAUCCCAGAAAGGUGAGAAA-3' (SEQ ID NO: 2695)
EGFR-2464 21 nt Target: 5'-GGAUCCCAGAAAGGUGAGAAAG-3' (SEQ ID NO: 2696)
EGFR-2465 21 nt Target: 5'-GAUCCCAGAAAGGUGAGAAAGU-3' (SEQ ID NO: 2697)
EGFR-2815 21 nt Target: 5'-CGCAGCAUGUCAAGAUCACAG-3' (SEQ ID NO: 2698)
EGFR-2816 21 nt Target: 5'-GCAGCAUGUCAAGAUCACAGA-3' (SEQ ID NO: 2699)
EGFR-2817 21 nt Target: 5'-CAGCAUGUCAAGAUCACAGAU-3' (SEQ ID NO: 2700)
EGFR-2818 21 nt Target: 5'-AGCAUGUCAAGAUCACAGAUU-3' (SEQ ID NO: 2701)
EGFR-2819 21 nt Target: 5'-GCAUGUCAAGAUCACAGAUUU-3' (SEQ ID NO: 2702)
EGFR-2820 21 nt Target: 5'-CAUGUCAAGAUCACAGAUUUU-3' (SEQ ID NO: 2703)
EGFR-2821 21 nt Target: 5'-AUGUCAAGAUCACAGAUUUUG-3' (SEQ ID NO: 2704)
EGFR-2822 21 nt Target: 5'-UGUCAAGAUCACAGAUUUUGG-3' (SEQ ID NO: 2705)
EGFR-2823 21 nt Target: 5'-GUCAAGAUCACAGAUUUUGGG-3' (SEQ ID NO: 2706)
EGFR-2824 21 nt Target: 5'-UCAAGAUCACAGAUUUUGGGC-3' (SEQ ID NO: 2707)
EGFR-2825 21 nt Target: 5'-CAAGAUCACAGAUUUUGGGCU-3' (SEQ ID NO: 2708)
EGFR-2826 21 nt Target: 5'-AAGAUCACAGAUUUUGGGCUG-3' (SEQ ID NO: 2709)
EGFR-2827 21 nt Target: 5'-AGAUCACAGAUUUUGGGCUGG-3' (SEQ ID NO: 2710)
EGFR-2828 21 nt Target: 5'-GAUCACAGAUUUUGGGCUGGC-3' (SEQ ID NO: 2711)
EGFR-2829 21 nt Target: 5'-AUCACAGAUUUUGGGCUGGCC-3' (SEQ ID NO: 2712)
EGFR-2830 21 nt Target: 5'-UCACAGAUUUUGGGCUGGCCA-3' (SEQ ID NO: 2713)
EGFR-2831 21 nt Target: 5'-CACAGAUUUUGGGCUGGCCAA-3' (SEQ ID NO: 2714)
EGFR-2832 21 nt Target: 5'-ACAGAUUUUGGGCUGGCCAAA-3' (SEQ ID NO: 2715)
EGFR-2833 21 nt Target: 5'-CAGAUUUUGGGCUGGCCAAAC-3' (SEQ ID NO: 2716)
EGFR-2834 21 nt Target: 5'-AGAUUUUGGGCUGGCCAAACU-3' (SEQ ID NO: 2717)
EGFR-2835 21 nt Target: 5'-GAUUUUUGGGCUGGCCAAACUG-3' (SEQ ID NO: 2718)
EGFR-2836 21 nt Target: 5'-AUUUUUGGGCUGGCCAAACUGC-3' (SEQ ID NO: 2719)
EGFR-2837 21 nt Target: 5'-UUUUUGGGCUGGCCAAACUGCU-3' (SEQ ID NO: 2720)
EGFR-2891 21 nt Target: 5'-AGGCAAAGUGCCUAUCAAGUG-3' (SEQ ID NO: 2721)
EGFR-2892 21 nt Target: 5'-GGCAAAGUGCCUAUCAAGUGG-3' (SEQ ID NO: 2722)
EGFR-2893 21 nt Target: 5'-GCAAAGUGCCUAUCAAGUGGA-3' (SEQ ID NO: 2723)
EGFR-2894 21 nt Target: 5'-CAAAGUGCCUAUCAAGUGGAU-3' (SEQ ID NO: 2724)
EGFR-2895 21 nt Target: 5'-AAAGUGCCUAUCAAGUGGAUG-3' (SEQ ID NO: 2725)
EGFR-2896 21 nt Target: 5'-AAGUGCCUAUCAAGUGGAUGG-3' (SEQ ID NO: 2726)
EGFR-2897 21 nt Target: 5'-AGUGCCUAUCAAGUGGAUGGC-3' (SEQ ID NO: 2727)
EGFR-3088 21 nt Target: 5'-GUACCAUCGAUGUCUACAUGA-3' (SEQ ID NO: 2728)
EGFR-3089 21 nt Target: 5'-UACCAUCGAUGUCUACAUGAU-3' (SEQ ID NO: 2729)
EGFR-3090 21 nt Target: 5'-ACCAUCGAUGUCUACAUGAUC-3' (SEQ ID NO: 2730)
EGFR-3091 21 nt Target: 5'-CCAUCGAUGUCUACAUGAUCA-3' (SEQ ID NO: 2731)

EGFR-3092 21 nt Target: 5'-CAUCGAUGUCUACAUGAUCAU-3' (SEQ ID NO: 2732)
 EGFR-3093 21 nt Target: 5'-AUCGAUGUCUACAUGAUCAUG-3' (SEQ ID NO: 2733)
 EGFR-3094 21 nt Target: 5'-UCGAUGUCUACAUGAUCAUGG-3' (SEQ ID NO: 2734)
 EGFR-3095 21 nt Target: 5'-CGAUGUCUACAUGAUCAUGGU-3' (SEQ ID NO: 2735)
 EGFR-3096 21 nt Target: 5'-GAUGUCUACAUGAUCAUGGUC-3' (SEQ ID NO: 2736)
 EGFR-3097 21 nt Target: 5'-AUGUCUACAUGAUCAUGGUCA-3' (SEQ ID NO: 2737)
 EGFR-3098 21 nt Target: 5'-UGUCUACAUGAUCAUGGUCAA-3' (SEQ ID NO: 2738)
 EGFR-3099 21 nt Target: 5'-GUCUACAUGAUCAUGGUCAAG-3' (SEQ ID NO: 2739)
 EGFR-3100 21 nt Target: 5'-UCUACAUGAUCAUGGUCAAGU-3' (SEQ ID NO: 2740)
 EGFR-3101 21 nt Target: 5'-CUACAUGAUCAUGGUCAAGUG-3' (SEQ ID NO: 2741)
 EGFR-3102 21 nt Target: 5'-UACAUGAUCAUGGUCAAGUGC-3' (SEQ ID NO: 2742)
 EGFR-3103 21 nt Target: 5'-ACAUGAUCAUGGUCAAGUGCU-3' (SEQ ID NO: 2743)
 EGFR-3104 21 nt Target: 5'-CAUGAUCAUGGUCAAGUGCUG-3' (SEQ ID NO: 2744)
 EGFR-3105 21 nt Target: 5'-AUGAUCAUGGUCAAGUGCUGG-3' (SEQ ID NO: 2745)
 EGFR-3106 21 nt Target: 5'-UGAUCAUGGUCAAGUGCUGGA-3' (SEQ ID NO: 2746)
 EGFR-3107 21 nt Target: 5'-GAUCAUGGUCAAGUGCUGGAU-3' (SEQ ID NO: 2747)
 EGFR-3108 21 nt Target: 5'-AUCAUGGUCAAGUGCUGGAUG-3' (SEQ ID NO: 2748)
 EGFR-3109 21 nt Target: 5'-UCAUGGUCAAGUGCUGGAUGA-3' (SEQ ID NO: 2749)
 EGFR-3110 21 nt Target: 5'-CAUGGUCAAGUGCUGGAUGAU-3' (SEQ ID NO: 2750)
 EGFR-3111 21 nt Target: 5'-AUGGUCAAGUGCUGGAUGAUA-3' (SEQ ID NO: 2751)
 EGFR-3112 21 nt Target: 5'-UGGUCAAGUGCUGGAUGAUAG-3' (SEQ ID NO: 2752)
 EGFR-3113 21 nt Target: 5'-GGUCAAGUGCUGGAUGAUAGA-3' (SEQ ID NO: 2753)
 EGFR-3169 21 nt Target: 5'-UCGAAUUCUCCAAAAUGGCC-3' (SEQ ID NO: 2754)
 EGFR-3170 21 nt Target: 5'-CGAAUUCUCCAAAAUGGCCG-3' (SEQ ID NO: 2755)
 EGFR-3220 21 nt Target: 5'-GGGAUGAAAGAAUGCAUUUGC-3' (SEQ ID NO: 2756)
 EGFR-3221 21 nt Target: 5'-GGAUGAAAGAAUGCAUUUGCC-3' (SEQ ID NO: 2757)
 EGFR-3222 21 nt Target: 5'-GAUGAAAGAAUGCAUUUGCCA-3' (SEQ ID NO: 2758)
 EGFR-3223 21 nt Target: 5'-AUGAAAGAAUGCAUUUGCCAA-3' (SEQ ID NO: 2759)
 EGFR-3224 21 nt Target: 5'-UGAAAGAAUGCAUUUGCCAAG-3' (SEQ ID NO: 2760)
 EGFR-3772 21 nt Target: 5'-UGGACAACCCUGACUACCAGC-3' (SEQ ID NO: 2761)
 EGFR-3773 21 nt Target: 5'-GGACAACCCUGACUACCAGCA-3' (SEQ ID NO: 2762)
 EGFR-3774 21 nt Target: 5'-GACAACCCUGACUACCAGCAG-3' (SEQ ID NO: 2763)
 EGFR-3775 21 nt Target: 5'-ACAACCCUGACUACCAGCAGG-3' (SEQ ID NO: 2764)
 EGFR-3776 21 nt Target: 5'-CAACCCUGACUACCAGCAGGA-3' (SEQ ID NO: 2765)
 EGFR-3777 21 nt Target: 5'-AACCCUGACUACCAGCAGGAC-3' (SEQ ID NO: 2766)
 EGFR-3778 21 nt Target: 5'-ACCCUGACUACCAGCAGGACU-3' (SEQ ID NO: 2767)
 EGFR-3779 21 nt Target: 5'-CCCUGACUACCAGCAGGACUU-3' (SEQ ID NO: 2768)

COMPONENT 19 NUCLEOTIDE TARGET mRNA SEQUENCES

EGFR-31 19 nt Target #1: 5'-CGCAGCGCGGCCGAGCAG-3' (SEQ ID NO: 2769)
 EGFR-31 19 nt Target #2: 5'-GCGCAGCGCGGCCGAGCA-3' (SEQ ID NO: 3029)
 EGFR-31 19 nt Target #3: 5'-GGCGCAGCGCGGCCGAGC-3' (SEQ ID NO: 3289)
 EGFR-32 19 nt Target #1: 5'-GCAGCGCGGCCGAGCAGC-3' (SEQ ID NO: 2770)
 EGFR-32 19 nt Target #2: 5'-CGCAGCGCGGCCGAGCAG-3' (SEQ ID NO: 3030)
 EGFR-32 19 nt Target #3: 5'-GCGCAGCGCGGCCGAGCA-3' (SEQ ID NO: 3290)
 EGFR-34 19 nt Target #1: 5'-AGCGCGGCCGAGCAGCCU-3' (SEQ ID NO: 2771)
 EGFR-34 19 nt Target #2: 5'-CAGCGCGGCCGAGCAGCC-3' (SEQ ID NO: 3031)
 EGFR-34 19 nt Target #3: 5'-GCAGCGCGGCCGAGCAGC-3' (SEQ ID NO: 3291)
 EGFR-298 19 nt Target #1: 5'-GCGCUCCUGGCGCUGCUGG-3' (SEQ ID NO: 2772)
 EGFR-298 19 nt Target #2: 5'-AGCGCUCCUGGCGCUGCUG-3' (SEQ ID NO: 3032)
 EGFR-298 19 nt Target #3: 5'-CAGCGCUCCUGGCGCUGCU-3' (SEQ ID NO: 3292)
 EGFR-300 19 nt Target #1: 5'-GCUCCUGGCGCUGCUGGCU-3' (SEQ ID NO: 2773)
 EGFR-300 19 nt Target #2: 5'-CGCUCCUGGCGCUGCUGGC-3' (SEQ ID NO: 3033)
 EGFR-300 19 nt Target #3: 5'-GCGCUCCUGGCGCUGCUGG-3' (SEQ ID NO: 3293)
 EGFR-302 19 nt Target #1: 5'-UCCUGGCGCUGCUGGCUGC-3' (SEQ ID NO: 2774)
 EGFR-302 19 nt Target #2: 5'-CUCCUGGCGCUGCUGGCUG-3' (SEQ ID NO: 3034)
 EGFR-302 19 nt Target #3: 5'-GCUCCUGGCGCUGCUGGCU-3' (SEQ ID NO: 3294)
 EGFR-390 19 nt Target #1: 5'-GUUGGGCACUUUGAAGAU-3' (SEQ ID NO: 2775)
 EGFR-390 19 nt Target #2: 5'-AGUUGGGCACUUUGAAGA-3' (SEQ ID NO: 3035)

EGFR-390 19 nt Target #3: 5'-CAGUUGGGCACUUUUGAAG-3' (SEQ ID NO: 3295)
EGFR-458 19 nt Target #1: 5'-GGAAUUUGGAAAUUACCUA-3' (SEQ ID NO: 2776)
EGFR-458 19 nt Target #2: 5'-GGGAAUUUGGAAAUUACCU-3' (SEQ ID NO: 3036)
EGFR-458 19 nt Target #3: 5'-UGGGAAUUUGGAAAUUACC-3' (SEQ ID NO: 3296)
EGFR-489 19 nt Target #1: 5'-UUAUGAUCUUUCCUUCUUA-3' (SEQ ID NO: 2777)
EGFR-489 19 nt Target #2: 5'-AUUAUGAUCUUUCCUUCUUA-3' (SEQ ID NO: 3037)
EGFR-489 19 nt Target #3: 5'-AAUUAUGAUCUUUCCUUCU-3' (SEQ ID NO: 3297)
EGFR-525 19 nt Target #1: 5'-GGCUGGUUAUGUCCUCAU-3' (SEQ ID NO: 2778)
EGFR-525 19 nt Target #2: 5'-UGGCUGGUUAUGUCCUCAU-3' (SEQ ID NO: 3038)
EGFR-525 19 nt Target #3: 5'-GUGGCUGGUUAUGUCCUCA-3' (SEQ ID NO: 3298)
EGFR-676 19 nt Target #1: 5'-CCCAUGAGAAAUUACAGG-3' (SEQ ID NO: 2779)
EGFR-676 19 nt Target #2: 5'-GCCCAUGAGAAAUUACAG-3' (SEQ ID NO: 3039)
EGFR-676 19 nt Target #3: 5'-UGCCCAUGAGAAAUUACA-3' (SEQ ID NO: 3299)
EGFR-701 19 nt Target #1: 5'-UGCAUGGCGCCGUGCGGUU-3' (SEQ ID NO: 2780)
EGFR-701 19 nt Target #2: 5'-CUGCAUGGCGCCGUGCGGU-3' (SEQ ID NO: 3040)
EGFR-701 19 nt Target #3: 5'-CCUGCAUGGCGCCGUGCGG-3' (SEQ ID NO: 3300)
EGFR-707 19 nt Target #1: 5'-GCGCCGUGCGGUUCAGCAA-3' (SEQ ID NO: 2781)
EGFR-707 19 nt Target #2: 5'-GGCGCCGUGCGGUUCAGCA-3' (SEQ ID NO: 3041)
EGFR-707 19 nt Target #3: 5'-UGGCGCCGUGCGGUUCAGC-3' (SEQ ID NO: 3301)
EGFR-707 19 nt Target #1: 5'-GCGCCGUGCGGUUCAGCAA-3' (SEQ ID NO: 2782)
EGFR-707 19 nt Target #2: 5'-GGCGCCGUGCGGUUCAGCA-3' (SEQ ID NO: 3042)
EGFR-707 19 nt Target #3: 5'-UGGCGCCGUGCGGUUCAGC-3' (SEQ ID NO: 3302)
EGFR-709 19 nt Target #1: 5'-GCCGUGCGGUUCAGCAACA-3' (SEQ ID NO: 2783)
EGFR-709 19 nt Target #2: 5'-CGCCGUGCGGUUCAGCAAC-3' (SEQ ID NO: 3043)
EGFR-709 19 nt Target #3: 5'-GCGCCGUGCGGUUCAGCAA-3' (SEQ ID NO: 3303)
EGFR-710 19 nt Target #1: 5'-CCGUGCGGUUCAGCAACAA-3' (SEQ ID NO: 2784)
EGFR-710 19 nt Target #2: 5'-GCCGUGCGGUUCAGCAACA-3' (SEQ ID NO: 3044)
EGFR-710 19 nt Target #3: 5'-CGCCGUGCGGUUCAGCAAC-3' (SEQ ID NO: 3304)
EGFR-827 19 nt Target #1: 5'-GCUGCCAAAAGUGUGAUCC-3' (SEQ ID NO: 2785)
EGFR-827 19 nt Target #2: 5'-AGCUGCCAAAAGUGUGAUC-3' (SEQ ID NO: 3045)
EGFR-827 19 nt Target #3: 5'-CAGCUGCCAAAAGUGUGAU-3' (SEQ ID NO: 3305)
EGFR-912 19 nt Target #1: 5'-CUGUGCCCAGCAGUGCUCC-3' (SEQ ID NO: 2786)
EGFR-912 19 nt Target #2: 5'-UCUGUGCCCAGCAGUGCUC-3' (SEQ ID NO: 3046)
EGFR-912 19 nt Target #3: 5'-AUCUGUGCCCAGCAGUGCU-3' (SEQ ID NO: 3306)
EGFR-914 19 nt Target #1: 5'-GUGCCCAGCAGUGCUCCGG-3' (SEQ ID NO: 2787)
EGFR-914 19 nt Target #2: 5'-UGUGCCCAGCAGUGCUCCG-3' (SEQ ID NO: 3047)
EGFR-914 19 nt Target #3: 5'-CUGUGCCCAGCAGUGCUCC-3' (SEQ ID NO: 3307)
EGFR-926 19 nt Target #1: 5'-GCUCCGGGCGCUGCCGUGG-3' (SEQ ID NO: 2788)
EGFR-926 19 nt Target #2: 5'-UGCUCGGGCGCUGCCGUG-3' (SEQ ID NO: 3048)
EGFR-926 19 nt Target #3: 5'-GUGCUCGGGCGCUGCCGU-3' (SEQ ID NO: 3308)
EGFR-1005 19 nt Target #1: 5'-GAGCGACUGCCUGGUCUGC-3' (SEQ ID NO: 2789)
EGFR-1005 19 nt Target #2: 5'-AGAGCGACUGCCUGGUCUG-3' (SEQ ID NO: 3049)
EGFR-1005 19 nt Target #3: 5'-GAGAGCGACUGCCUGGUCU-3' (SEQ ID NO: 3309)
EGFR-1013 19 nt Target #1: 5'-GCCUGGUCUGCCGCAAAU-3' (SEQ ID NO: 2790)
EGFR-1013 19 nt Target #2: 5'-UGCCUGGUCUGCCGCAAAU-3' (SEQ ID NO: 3050)
EGFR-1013 19 nt Target #3: 5'-CUGCCUGGUCUGCCGCAAA-3' (SEQ ID NO: 3310)
EGFR-1175 19 nt Target #1: 5'-CAGAUCACGGCUCGUGCGU-3' (SEQ ID NO: 2791)
EGFR-1175 19 nt Target #2: 5'-ACAGAUCACGGCUCGUGCG-3' (SEQ ID NO: 3051)
EGFR-1175 19 nt Target #3: 5'-GACAGAUCACGGCUCGUGC-3' (SEQ ID NO: 3311)
EGFR-1271 19 nt Target #1: 5'-GCAAAGUGUGUAACGGAAU-3' (SEQ ID NO: 2792)
EGFR-1271 19 nt Target #2: 5'-CGCAAAGUGUGUAACGGAA-3' (SEQ ID NO: 3052)
EGFR-1271 19 nt Target #3: 5'-CCGCAAAGUGUGUAACGGA-3' (SEQ ID NO: 3312)
EGFR-1286 19 nt Target #1: 5'-GAAUAGGUUAUUGGUGAAU-3' (SEQ ID NO: 2793)
EGFR-1286 19 nt Target #2: 5'-GGAAUAGGUUAUUGGUGAAU-3' (SEQ ID NO: 3053)
EGFR-1286 19 nt Target #3: 5'-CGGAAUAGGUUAUUGGUGAA-3' (SEQ ID NO: 3313)
EGFR-1330 19 nt Target #1: 5'-ACGAAUAUUAACACUUCA-3' (SEQ ID NO: 2794)
EGFR-1330 19 nt Target #2: 5'-UACGAAUAUUAACACUUC-3' (SEQ ID NO: 3054)
EGFR-1330 19 nt Target #3: 5'-UACGAAUAUUAACACUU-3' (SEQ ID NO: 3314)
EGFR-1437 19 nt Target #1: 5'-ACAGGAACUGGAUAUUCUG-3' (SEQ ID NO: 2795)

EGFR-1437 19 nt Target #2: 5'-CACAGGAACUGGAUAUUCU-3' (SEQ ID NO: 3055)
 EGFR-1437 19 nt Target #3: 5'-CCACAGGAACUGGAUAUUC-3' (SEQ ID NO: 3315)
 EGFR-1475 19 nt Target #1: 5'-CAGGGUUUUUGCUGAUUCA-3' (SEQ ID NO: 2796)
 EGFR-1475 19 nt Target #2: 5'-ACAGGGUUUUUGCUGAUUC-3' (SEQ ID NO: 3056)
 EGFR-1475 19 nt Target #3: 5'-CACAGGGUUUUUGCUGAUU-3' (SEQ ID NO: 3316)
 EGFR-1661 19 nt Target #1: 5'-CAGGAAACAAAAUUUGUG-3' (SEQ ID NO: 2797)
 EGFR-1661 19 nt Target #2: 5'-UCAGGAAACAAAAUUUGU-3' (SEQ ID NO: 3057)
 EGFR-1661 19 nt Target #3: 5'-UUCAGGAAACAAAAUUUG-3' (SEQ ID NO: 3317)
 EGFR-1679 19 nt Target #1: 5'-GCUAUGCAAAUACAAUAAA-3' (SEQ ID NO: 2798)
 EGFR-1679 19 nt Target #2: 5'-UGCUAUGCAAAUACAAUAA-3' (SEQ ID NO: 3058)
 EGFR-1679 19 nt Target #3: 5'-GUGCUAUGCAAAUACAAUA-3' (SEQ ID NO: 3318)
 EGFR-1723 19 nt Target #1: 5'-GGUCAGAAAACCAAAUUA-3' (SEQ ID NO: 2799)
 EGFR-1723 19 nt Target #2: 5'-CGGUCAGAAAACCAAAUU-3' (SEQ ID NO: 3059)
 EGFR-1723 19 nt Target #3: 5'-CCGGUCAGAAAACCAAAU-3' (SEQ ID NO: 3319)
 EGFR-1838 19 nt Target #1: 5'-GCGUCUCUUGCCGGAAUGU-3' (SEQ ID NO: 2800)
 EGFR-1838 19 nt Target #2: 5'-UGCGUCUCUUGCCGGAAUG-3' (SEQ ID NO: 3060)
 EGFR-1838 19 nt Target #3: 5'-CUGCGUCUCUUGCCGGAAU-3' (SEQ ID NO: 3320)
 EGFR-2227 19 nt Target #1: 5'-GCCCUCUCUUGCUGCUGG-3' (SEQ ID NO: 2801)
 EGFR-2227 19 nt Target #2: 5'-GGCCCUCUCUUGCUGCUG-3' (SEQ ID NO: 3061)
 EGFR-2227 19 nt Target #3: 5'-GGGCCCUCUCUUGCUGCU-3' (SEQ ID NO: 3321)
 EGFR-2228 19 nt Target #1: 5'-CCCUCCUCUUGCUGCUGGU-3' (SEQ ID NO: 2802)
 EGFR-2228 19 nt Target #2: 5'-GCCCUCCUCUUGCUGCUGG-3' (SEQ ID NO: 3062)
 EGFR-2228 19 nt Target #3: 5'-GGCCCUCCUCUUGCUGCUG-3' (SEQ ID NO: 3322)
 EGFR-2232 19 nt Target #1: 5'-CCUCUUGCUGCUGGUGGUG-3' (SEQ ID NO: 2803)
 EGFR-2232 19 nt Target #2: 5'-UCCUCUUGCUGCUGGUGGU-3' (SEQ ID NO: 3063)
 EGFR-2232 19 nt Target #3: 5'-CUCCUCUUGCUGCUGGUGG-3' (SEQ ID NO: 3323)
 EGFR-2233 19 nt Target #1: 5'-CUCUUGCUGCUGGUGGUGG-3' (SEQ ID NO: 2804)
 EGFR-2233 19 nt Target #2: 5'-CCUCUUGCUGCUGGUGGUG-3' (SEQ ID NO: 3064)
 EGFR-2233 19 nt Target #3: 5'-UCCUCUUGCUGCUGGUGGU-3' (SEQ ID NO: 3324)
 EGFR-2295 19 nt Target #1: 5'-GAAGCGCACGCUGCGGAGG-3' (SEQ ID NO: 2805)
 EGFR-2295 19 nt Target #2: 5'-GGAAGCGCACGCUGCGGAG-3' (SEQ ID NO: 3065)
 EGFR-2295 19 nt Target #3: 5'-CGGAAGCGCACGCUGCGGA-3' (SEQ ID NO: 3325)
 EGFR-2298 19 nt Target #1: 5'-GCGCACGCUGCGGAGGCUG-3' (SEQ ID NO: 2806)
 EGFR-2298 19 nt Target #2: 5'-AGCGCACGCUGCGGAGGCU-3' (SEQ ID NO: 3066)
 EGFR-2298 19 nt Target #3: 5'-AAGCGCACGCUGCGGAGGC-3' (SEQ ID NO: 3326)
 EGFR-2399 19 nt Target #1: 5'-CUGAAUUCAAAAAGAUCAA-3' (SEQ ID NO: 2807)
 EGFR-2399 19 nt Target #2: 5'-ACUGAAUUCAAAAAGAUCA-3' (SEQ ID NO: 3067)
 EGFR-2399 19 nt Target #3: 5'-AACUGAAUUCAAAAAGAUC-3' (SEQ ID NO: 3327)
 EGFR-2417 19 nt Target #1: 5'-AAGUGCUGGGCUCCGGUGC-3' (SEQ ID NO: 2808)
 EGFR-2417 19 nt Target #2: 5'-AAAGUGCUGGGCUCCGGUG-3' (SEQ ID NO: 3068)
 EGFR-2417 19 nt Target #3: 5'-CAAAGUGCUGGGCUCCGGU-3' (SEQ ID NO: 3328)
 EGFR-2419 19 nt Target #1: 5'-GUGCUGGGCUCCGGUGCGU-3' (SEQ ID NO: 2809)
 EGFR-2419 19 nt Target #2: 5'-AGUGCUGGGCUCCGGUGCG-3' (SEQ ID NO: 3069)
 EGFR-2419 19 nt Target #3: 5'-AAGUGCUGGGCUCCGGUGC-3' (SEQ ID NO: 3329)
 EGFR-2420 19 nt Target #1: 5'-UGCUGGGCUCCGGUGCGUU-3' (SEQ ID NO: 2810)
 EGFR-2420 19 nt Target #2: 5'-GUGCUGGGCUCCGGUGCGU-3' (SEQ ID NO: 3070)
 EGFR-2420 19 nt Target #3: 5'-AGUGCUGGGCUCCGGUGCG-3' (SEQ ID NO: 3330)
 EGFR-2421 19 nt Target #1: 5'-GCUGGGCUCCGGUGCGUUC-3' (SEQ ID NO: 2811)
 EGFR-2421 19 nt Target #2: 5'-UGCUGGGCUCCGGUGCGUU-3' (SEQ ID NO: 3071)
 EGFR-2421 19 nt Target #3: 5'-GUGCUGGGCUCCGGUGCGU-3' (SEQ ID NO: 3331)
 EGFR-2422 19 nt Target #1: 5'-CUGGGCUCCGGUGCGUUCG-3' (SEQ ID NO: 2812)
 EGFR-2422 19 nt Target #2: 5'-GCUGGGCUCCGGUGCGUUC-3' (SEQ ID NO: 3072)
 EGFR-2422 19 nt Target #3: 5'-UGCUGGGCUCCGGUGCGUU-3' (SEQ ID NO: 3332)
 EGFR-2591 19 nt Target #1: 5'-UGUGCCGCCUGCUGGGCAU-3' (SEQ ID NO: 2813)
 EGFR-2591 19 nt Target #2: 5'-GUGUGCCGCCUGCUGGGCA-3' (SEQ ID NO: 3073)
 EGFR-2591 19 nt Target #3: 5'-CGUGUGCCGCCUGCUGGGC-3' (SEQ ID NO: 3333)
 EGFR-2592 19 nt Target #1: 5'-UGGCCGCCUGCUGGGCAUC-3' (SEQ ID NO: 2814)
 EGFR-2592 19 nt Target #2: 5'-UGUGCCGCCUGCUGGGCAU-3' (SEQ ID NO: 3074)
 EGFR-2592 19 nt Target #3: 5'-GUGUGCCGCCUGCUGGGCA-3' (SEQ ID NO: 3334)

EGFR-2594 19 nt Target #1: 5'-GCCGCCUGCUGGGCAUCUG-3' (SEQ ID NO: 2815)
 EGFR-2594 19 nt Target #2: 5'-UGCCGCCUGCUGGGCAUCU-3' (SEQ ID NO: 3075)
 EGFR-2594 19 nt Target #3: 5'-GUGCCGCCUGCUGGGCAUC-3' (SEQ ID NO: 3335)
 EGFR-2624 19 nt Target #1: 5'-CCGUGCAGCUCAUCACGCA-3' (SEQ ID NO: 2816)
 EGFR-2624 19 nt Target #2: 5'-ACCGUGCAGCUCAUCACGC-3' (SEQ ID NO: 3076)
 EGFR-2624 19 nt Target #3: 5'-CACCUGCAGCUCAUCACG-3' (SEQ ID NO: 3336)
 EGFR-2627 19 nt Target #1: 5'-UGCAGCUCAUCACGCAGCU-3' (SEQ ID NO: 2817)
 EGFR-2627 19 nt Target #2: 5'-GUGCAGCUCAUCACGCAGC-3' (SEQ ID NO: 3077)
 EGFR-2627 19 nt Target #3: 5'-CGUGCAGCUCAUCACGCAG-3' (SEQ ID NO: 3337)
 EGFR-2631 19 nt Target #1: 5'-GCUCAUCACGCAGCUCAUG-3' (SEQ ID NO: 2818)
 EGFR-2631 19 nt Target #2: 5'-AGCUCAUCACGCAGCUCAU-3' (SEQ ID NO: 3078)
 EGFR-2631 19 nt Target #3: 5'-CAGCUCAUCACGCAGCUCA-3' (SEQ ID NO: 3338)
 EGFR-2632 19 nt Target #1: 5'-CUCAUCACGCAGCUCAUGC-3' (SEQ ID NO: 2819)
 EGFR-2632 19 nt Target #2: 5'-GCUCAUCACGCAGCUCAUG-3' (SEQ ID NO: 3079)
 EGFR-2632 19 nt Target #3: 5'-AGCUCAUCACGCAGCUCAU-3' (SEQ ID NO: 3339)
 EGFR-2643 19 nt Target #1: 5'-GCUCAUGCCCUUCGGCUGC-3' (SEQ ID NO: 2820)
 EGFR-2643 19 nt Target #2: 5'-AGCUCAUGCCCUUCGGCUG-3' (SEQ ID NO: 3080)
 EGFR-2643 19 nt Target #3: 5'-CAGCUCAUGCCCUUCGGCU-3' (SEQ ID NO: 3340)
 EGFR-2644 19 nt Target #1: 5'-CUCAUGCCCUUCGGCUGCC-3' (SEQ ID NO: 2821)
 EGFR-2644 19 nt Target #2: 5'-GCUCAUGCCCUUCGGCUGC-3' (SEQ ID NO: 3081)
 EGFR-2644 19 nt Target #3: 5'-AGCUCAUGCCCUUCGGCUG-3' (SEQ ID NO: 3341)
 EGFR-2754 19 nt Target #1: 5'-GGAGGACCGUCGCUUGGUG-3' (SEQ ID NO: 2822)
 EGFR-2754 19 nt Target #2: 5'-UGGAGGACCGUCGCUUGGU-3' (SEQ ID NO: 3082)
 EGFR-2754 19 nt Target #3: 5'-UUGGAGGACCGUCGCUUGG-3' (SEQ ID NO: 3342)
 EGFR-2756 19 nt Target #1: 5'-AGGACCGUCGCUUGGUGCA-3' (SEQ ID NO: 2823)
 EGFR-2756 19 nt Target #2: 5'-GAGGACCGUCGCUUGGUGC-3' (SEQ ID NO: 3083)
 EGFR-2756 19 nt Target #3: 5'-GGAGGACCGUCGCUUGGUG-3' (SEQ ID NO: 3343)
 EGFR-2757 19 nt Target #1: 5'-GGACCGUCGCUUGGUGCAC-3' (SEQ ID NO: 2824)
 EGFR-2757 19 nt Target #2: 5'-AGGACCGUCGCUUGGUGCA-3' (SEQ ID NO: 3084)
 EGFR-2757 19 nt Target #3: 5'-GAGGACCGUCGCUUGGUGC-3' (SEQ ID NO: 3344)
 EGFR-2758 19 nt Target #1: 5'-GACCGUCGCUUGGUGCACC-3' (SEQ ID NO: 2825)
 EGFR-2758 19 nt Target #2: 5'-GGACCGUCGCUUGGUGCAC-3' (SEQ ID NO: 3085)
 EGFR-2758 19 nt Target #3: 5'-AGGACCGUCGCUUGGUGCA-3' (SEQ ID NO: 3345)
 EGFR-2760 19 nt Target #1: 5'-CCGUCGCUUGGUGCACC GC-3' (SEQ ID NO: 2826)
 EGFR-2760 19 nt Target #2: 5'-ACCGUCGCUUGGUGCACC G-3' (SEQ ID NO: 3086)
 EGFR-2760 19 nt Target #3: 5'-GACCGUCGCUUGGUGCACC-3' (SEQ ID NO: 3346)
 EGFR-2762 19 nt Target #1: 5'-GUCGCUUGGUGCACC GCGA-3' (SEQ ID NO: 2827)
 EGFR-2762 19 nt Target #2: 5'-CGUCGCUUGGUGCACC GCG-3' (SEQ ID NO: 3087)
 EGFR-2762 19 nt Target #3: 5'-CCGUCGCUUGGUGCACC GC-3' (SEQ ID NO: 3347)
 EGFR-2764 19 nt Target #1: 5'-CGCUUGGUGCACC GCGACC-3' (SEQ ID NO: 2828)
 EGFR-2764 19 nt Target #2: 5'-UCGCUUGGUGCACC GCGAC-3' (SEQ ID NO: 3088)
 EGFR-2764 19 nt Target #3: 5'-GUCGCUUGGUGCACC GCGA-3' (SEQ ID NO: 3348)
 EGFR-2765 19 nt Target #1: 5'-GCUUGGUGCACC GCGACCU-3' (SEQ ID NO: 2829)
 EGFR-2765 19 nt Target #2: 5'-CGCUUGGUGCACC GCGACC-3' (SEQ ID NO: 3089)
 EGFR-2765 19 nt Target #3: 5'-UCGCUUGGUGCACC GCGAC-3' (SEQ ID NO: 3349)
 EGFR-2767 19 nt Target #1: 5'-UUGGUGCACC GCGACCUGG-3' (SEQ ID NO: 2830)
 EGFR-2767 19 nt Target #2: 5'-CUUGGUGCACC GCGACCUG-3' (SEQ ID NO: 3090)
 EGFR-2767 19 nt Target #3: 5'-GCUUGGUGCACC GCGACCU-3' (SEQ ID NO: 3350)
 EGFR-2915 19 nt Target #1: 5'-CAUUGGAAUCAAUUUUACA-3' (SEQ ID NO: 2831)
 EGFR-2915 19 nt Target #2: 5'-GCAUUGGAAUCAAUUUUAC-3' (SEQ ID NO: 3091)
 EGFR-2915 19 nt Target #3: 5'-GGCAUUGGAAUCAAUUUUA-3' (SEQ ID NO: 3351)
 EGFR-3115 19 nt Target #1: 5'-AAGUGCUGGAUGAUAGACG-3' (SEQ ID NO: 2832)
 EGFR-3115 19 nt Target #2: 5'-CAAGUGCUGGAUGAUAGAC-3' (SEQ ID NO: 3092)
 EGFR-3115 19 nt Target #3: 5'-UCAAGUGCUGGAUGAUAGA-3' (SEQ ID NO: 3352)
 EGFR-3117 19 nt Target #1: 5'-GUGCUGGAUGAUAGACGCA-3' (SEQ ID NO: 2833)
 EGFR-3117 19 nt Target #2: 5'-AGUGCUGGAUGAUAGACGC-3' (SEQ ID NO: 3093)
 EGFR-3117 19 nt Target #3: 5'-AAGUGCUGGAUGAUAGACG-3' (SEQ ID NO: 3353)
 EGFR-3118 19 nt Target #1: 5'-UGCUGGAUGAUAGACGCAG-3' (SEQ ID NO: 2834)
 EGFR-3118 19 nt Target #2: 5'-GUGCUGGAUGAUAGACGCA-3' (SEQ ID NO: 3094)

EGFR-3118 19 nt Target #3: 5'-AGUGCUGGAUGAUAGACGC-3' (SEQ ID NO: 3354)
 EGFR-3120 19 nt Target #1: 5'-CUGGAUGAUAGACGCAGAU-3' (SEQ ID NO: 2835)
 EGFR-3120 19 nt Target #2: 5'-GCUGGAUGAUAGACGCAGA-3' (SEQ ID NO: 3095)
 EGFR-3120 19 nt Target #3: 5'-UGCUGGAUGAUAGACGCAG-3' (SEQ ID NO: 3355)
 EGFR-3372 19 nt Target #1: 5'-CCUGAGCUCUCUGAGUGCA-3' (SEQ ID NO: 2836)
 EGFR-3372 19 nt Target #2: 5'-UCCUGAGCUCUCUGAGUGC-3' (SEQ ID NO: 3096)
 EGFR-3372 19 nt Target #3: 5'-CUCCUGAGCUCUCUGAGUG-3' (SEQ ID NO: 3356)
 EGFR-3375 19 nt Target #1: 5'-GAGCUCUCUGAGUGCAACC-3' (SEQ ID NO: 2837)
 EGFR-3375 19 nt Target #2: 5'-UGAGCUCUCUGAGUGCAAC-3' (SEQ ID NO: 3097)
 EGFR-3375 19 nt Target #3: 5'-CUGAGCUCUCUGAGUGCAA-3' (SEQ ID NO: 3357)
 EGFR-3440 19 nt Target #1: 5'-GCUGUCCCAUCAAGGAAGA-3' (SEQ ID NO: 2838)
 EGFR-3440 19 nt Target #2: 5'-AGCUGUCCCAUCAAGGAAG-3' (SEQ ID NO: 3098)
 EGFR-3440 19 nt Target #3: 5'-AAGCUGUCCCAUCAAGGAA-3' (SEQ ID NO: 3358)
 EGFR-3441 19 nt Target #1: 5'-CUGUCCCAUCAAGGAAGAC-3' (SEQ ID NO: 2839)
 EGFR-3441 19 nt Target #2: 5'-GCUGUCCCAUCAAGGAAGA-3' (SEQ ID NO: 3099)
 EGFR-3441 19 nt Target #3: 5'-AGCUGUCCCAUCAAGGAAG-3' (SEQ ID NO: 3359)
 EGFR-3457 19 nt Target #1: 5'-GACAGCUUCUUGCAGCGAU-3' (SEQ ID NO: 2840)
 EGFR-3457 19 nt Target #2: 5'-AGACAGCUUCUUGCAGCGA-3' (SEQ ID NO: 3100)
 EGFR-3457 19 nt Target #3: 5'-AAGACAGCUUCUUGCAGCG-3' (SEQ ID NO: 3360)
 EGFR-3458 19 nt Target #1: 5'-ACAGCUUCUUGCAGCGAUA-3' (SEQ ID NO: 2841)
 EGFR-3458 19 nt Target #2: 5'-GACAGCUUCUUGCAGCGAU-3' (SEQ ID NO: 3101)
 EGFR-3458 19 nt Target #3: 5'-AGACAGCUUCUUGCAGCGA-3' (SEQ ID NO: 3361)
 EGFR-3459 19 nt Target #1: 5'-CAGCUUCUUGCAGCGAUAC-3' (SEQ ID NO: 2842)
 EGFR-3459 19 nt Target #2: 5'-ACAGCUUCUUGCAGCGAUA-3' (SEQ ID NO: 3102)
 EGFR-3459 19 nt Target #3: 5'-GACAGCUUCUUGCAGCGAU-3' (SEQ ID NO: 3362)
 EGFR-3460 19 nt Target #1: 5'-AGCUUCUUGCAGCGAUACA-3' (SEQ ID NO: 2843)
 EGFR-3460 19 nt Target #2: 5'-CAGCUUCUUGCAGCGAUAC-3' (SEQ ID NO: 3103)
 EGFR-3460 19 nt Target #3: 5'-ACAGCUUCUUGCAGCGAUA-3' (SEQ ID NO: 3363)
 EGFR-3461 19 nt Target #1: 5'-GCUUCUUGCAGCGAUACAG-3' (SEQ ID NO: 2844)
 EGFR-3461 19 nt Target #2: 5'-AGCUUCUUGCAGCGAUACA-3' (SEQ ID NO: 3104)
 EGFR-3461 19 nt Target #3: 5'-CAGCUUCUUGCAGCGAUAC-3' (SEQ ID NO: 3364)
 EGFR-3463 19 nt Target #1: 5'-UUCUUGCAGCGAUACAGCU-3' (SEQ ID NO: 2845)
 EGFR-3463 19 nt Target #2: 5'-CUUCUUGCAGCGAUACAGC-3' (SEQ ID NO: 3105)
 EGFR-3463 19 nt Target #3: 5'-GCUUCUUGCAGCGAUACAG-3' (SEQ ID NO: 3365)
 EGFR-3876 19 nt Target #1: 5'-ACAAAGCAGUGAAUUUAUU-3' (SEQ ID NO: 2846)
 EGFR-3876 19 nt Target #2: 5'-CACAAAGCAGUGAAUUUAU-3' (SEQ ID NO: 3106)
 EGFR-3876 19 nt Target #3: 5'-CCACAAAGCAGUGAAUUUA-3' (SEQ ID NO: 3366)
 EGFR-4178 19 nt Target #1: 5'-AUUUUUUAAAAAAAAAAAA-3' (SEQ ID NO: 2847)
 EGFR-4178 19 nt Target #2: 5'-UAUUUUUAAAAAAAAAAAA-3' (SEQ ID NO: 3107)
 EGFR-4178 19 nt Target #3: 5'-GUUUUUUAAAAAAAAAAAA-3' (SEQ ID NO: 3367)
 EGFR-4205 19 nt Target #1: 5'-UGAGGAUUUUUAUUGAUUG-3' (SEQ ID NO: 2848)
 EGFR-4205 19 nt Target #2: 5'-GUGAGGAUUUUUAUUGAUU-3' (SEQ ID NO: 3108)
 EGFR-4205 19 nt Target #3: 5'-UGUGAGGAUUUUUAUUGAU-3' (SEQ ID NO: 3368)
 EGFR-4249 19 nt Target #1: 5'-CUAUUGAUUUUUACUUCAA-3' (SEQ ID NO: 2849)
 EGFR-4249 19 nt Target #2: 5'-GCUAUUGAUUUUUACUUCA-3' (SEQ ID NO: 3109)
 EGFR-4249 19 nt Target #3: 5'-CGCUAUUGAUUUUUACUUC-3' (SEQ ID NO: 3369)
 EGFR-4284 19 nt Target #1: 5'-GGAAGAAGCUUGCUGGUAG-3' (SEQ ID NO: 2850)
 EGFR-4284 19 nt Target #2: 5'-AGGAAGAAGCUUGCUGGUA-3' (SEQ ID NO: 3110)
 EGFR-4284 19 nt Target #3: 5'-AAGGAAGAAGCUUGCUGGU-3' (SEQ ID NO: 3370)
 EGFR-4285 19 nt Target #1: 5'-GAAGAAGCUUGCUGGUAGC-3' (SEQ ID NO: 2851)
 EGFR-4285 19 nt Target #2: 5'-GGAAGAAGCUUGCUGGUAG-3' (SEQ ID NO: 3111)
 EGFR-4285 19 nt Target #3: 5'-AGGAAGAAGCUUGCUGGUA-3' (SEQ ID NO: 3371)
 EGFR-4286 19 nt Target #1: 5'-AAGAAGCUUGCUGGUAGCA-3' (SEQ ID NO: 2852)
 EGFR-4286 19 nt Target #2: 5'-GAAGAAGCUUGCUGGUAGC-3' (SEQ ID NO: 3112)
 EGFR-4286 19 nt Target #3: 5'-GGAAGAAGCUUGCUGGUAG-3' (SEQ ID NO: 3372)
 EGFR-4287 19 nt Target #1: 5'-AGAAGCUUGCUGGUAGCAC-3' (SEQ ID NO: 2853)
 EGFR-4287 19 nt Target #2: 5'-AAGAAGCUUGCUGGUAGCA-3' (SEQ ID NO: 3113)
 EGFR-4287 19 nt Target #3: 5'-GAAGAAGCUUGCUGGUAGC-3' (SEQ ID NO: 3373)
 EGFR-4288 19 nt Target #1: 5'-GAAGCUUGCUGGUAGCACU-3' (SEQ ID NO: 2854)

EGFR-4288 19 nt Target #2: 5'-AGAAGCUUGCUGGUAGCAC-3' (SEQ ID NO: 3114)
EGFR-4288 19 nt Target #3: 5'-AAGAAGCUUGCUGGUAGCA-3' (SEQ ID NO: 3374)
EGFR-4290 19 nt Target #1: 5'-AGCUUGCUGGUAGCACUUG-3' (SEQ ID NO: 2855)
EGFR-4290 19 nt Target #2: 5'-AAGCUUGCUGGUAGCACUU-3' (SEQ ID NO: 3115)
EGFR-4290 19 nt Target #3: 5'-GAAGCUUGCUGGUAGCACU-3' (SEQ ID NO: 3375)
EGFR-4291 19 nt Target #1: 5'-GCUUGCUGGUAGCACUUGC-3' (SEQ ID NO: 2856)
EGFR-4291 19 nt Target #2: 5'-AGCUUGCUGGUAGCACUUG-3' (SEQ ID NO: 3116)
EGFR-4291 19 nt Target #3: 5'-AAGCUUGCUGGUAGCACUU-3' (SEQ ID NO: 3376)
EGFR-4292 19 nt Target #1: 5'-CUUGCUGGUAGCACUUGC-3' (SEQ ID NO: 2857)
EGFR-4292 19 nt Target #2: 5'-GCUUGCUGGUAGCACUUGC-3' (SEQ ID NO: 3117)
EGFR-4292 19 nt Target #3: 5'-AGCUUGCUGGUAGCACUUG-3' (SEQ ID NO: 3377)
EGFR-4293 19 nt Target #1: 5'-UUGCUGGUAGCACUUGC-3' (SEQ ID NO: 2858)
EGFR-4293 19 nt Target #2: 5'-CUUGCUGGUAGCACUUGC-3' (SEQ ID NO: 3118)
EGFR-4293 19 nt Target #3: 5'-GCUUGCUGGUAGCACUUGC-3' (SEQ ID NO: 3378)
EGFR-4294 19 nt Target #1: 5'-UGCUGGUAGCACUUGC-3' (SEQ ID NO: 2859)
EGFR-4294 19 nt Target #2: 5'-UUGCUGGUAGCACUUGC-3' (SEQ ID NO: 3119)
EGFR-4294 19 nt Target #3: 5'-CUUGCUGGUAGCACUUGC-3' (SEQ ID NO: 3379)
EGFR-4295 19 nt Target #1: 5'-GCUGGUAGCACUUGC-3' (SEQ ID NO: 2860)
EGFR-4295 19 nt Target #2: 5'-UGCUGGUAGCACUUGC-3' (SEQ ID NO: 3120)
EGFR-4295 19 nt Target #3: 5'-UUGCUGGUAGCACUUGC-3' (SEQ ID NO: 3380)
EGFR-4372 19 nt Target #1: 5'-AUGCUUGAUUCCAGUGGU-3' (SEQ ID NO: 2861)
EGFR-4372 19 nt Target #2: 5'-GAUGCUUGAUUCCAGUGGU-3' (SEQ ID NO: 3121)
EGFR-4372 19 nt Target #3: 5'-GGAUGCUUGAUUCCAGUGG-3' (SEQ ID NO: 3381)
EGFR-4373 19 nt Target #1: 5'-UGCUUGAUUCCAGUGGU-3' (SEQ ID NO: 2862)
EGFR-4373 19 nt Target #2: 5'-AUGCUUGAUUCCAGUGGU-3' (SEQ ID NO: 3122)
EGFR-4373 19 nt Target #3: 5'-GAUGCUUGAUUCCAGUGGU-3' (SEQ ID NO: 3382)
EGFR-4450 19 nt Target #1: 5'-CAGGCCGGAUCGGUACUG-3' (SEQ ID NO: 2863)
EGFR-4450 19 nt Target #2: 5'-GCAGGCCGGAUCGGUACUG-3' (SEQ ID NO: 3123)
EGFR-4450 19 nt Target #3: 5'-AGCAGGCCGGAUCGGUACU-3' (SEQ ID NO: 3383)
EGFR-4455 19 nt Target #1: 5'-CGGAUCGGUACUGUAUCAA-3' (SEQ ID NO: 2864)
EGFR-4455 19 nt Target #2: 5'-CCGGAUCGGUACUGUAUCA-3' (SEQ ID NO: 3124)
EGFR-4455 19 nt Target #3: 5'-GCCGGAUCGGUACUGUAUC-3' (SEQ ID NO: 3384)
EGFR-4550 19 nt Target #1: 5'-CUUAGACUUACUUUUGUA-3' (SEQ ID NO: 2865)
EGFR-4550 19 nt Target #2: 5'-CCUUAGACUUACUUUUGUA-3' (SEQ ID NO: 3125)
EGFR-4550 19 nt Target #3: 5'-UCCUAGACUUACUUUUGU-3' (SEQ ID NO: 3385)
EGFR-4684 19 nt Target #1: 5'-GUCUUGCUGUCAUGAAAUC-3' (SEQ ID NO: 2866)
EGFR-4684 19 nt Target #2: 5'-UGUCUUGCUGUCAUGAAAU-3' (SEQ ID NO: 3126)
EGFR-4684 19 nt Target #3: 5'-CUGUCUUGCUGUCAUGAAA-3' (SEQ ID NO: 3386)
EGFR-4804 19 nt Target #1: 5'-UAAGGAUAGCACCGCUUUU-3' (SEQ ID NO: 2867)
EGFR-4804 19 nt Target #2: 5'-CUAAGGAUAGCACCGCUUU-3' (SEQ ID NO: 3127)
EGFR-4804 19 nt Target #3: 5'-CCUAAGGAUAGCACCGCUU-3' (SEQ ID NO: 3387)
EGFR-4806 19 nt Target #1: 5'-AGGAUAGCACCGCUUUUGU-3' (SEQ ID NO: 2868)
EGFR-4806 19 nt Target #2: 5'-AAGGAUAGCACCGCUUUUG-3' (SEQ ID NO: 3128)
EGFR-4806 19 nt Target #3: 5'-UAAGGAUAGCACCGCUUUU-3' (SEQ ID NO: 3388)
EGFR-4807 19 nt Target #1: 5'-GGAUAGCACCGCUUUUGUU-3' (SEQ ID NO: 2869)
EGFR-4807 19 nt Target #2: 5'-AGGAUAGCACCGCUUUUGU-3' (SEQ ID NO: 3129)
EGFR-4807 19 nt Target #3: 5'-AAGGAUAGCACCGCUUUUG-3' (SEQ ID NO: 3389)
EGFR-4808 19 nt Target #1: 5'-GAUAGCACCGCUUUUGUUC-3' (SEQ ID NO: 2870)
EGFR-4808 19 nt Target #2: 5'-GGAUAGCACCGCUUUUGUU-3' (SEQ ID NO: 3130)
EGFR-4808 19 nt Target #3: 5'-AGGAUAGCACCGCUUUUGU-3' (SEQ ID NO: 3390)
EGFR-4809 19 nt Target #1: 5'-AUAGCACCGCUUUUGUUCU-3' (SEQ ID NO: 2871)
EGFR-4809 19 nt Target #2: 5'-GAUAGCACCGCUUUUGUUC-3' (SEQ ID NO: 3131)
EGFR-4809 19 nt Target #3: 5'-GGAUAGCACCGCUUUUGUU-3' (SEQ ID NO: 3391)
EGFR-4810 19 nt Target #1: 5'-UAGCACCGCUUUUGUUCUC-3' (SEQ ID NO: 2872)
EGFR-4810 19 nt Target #2: 5'-AUAGCACCGCUUUUGUUCU-3' (SEQ ID NO: 3132)
EGFR-4810 19 nt Target #3: 5'-GAUAGCACCGCUUUUGUUC-3' (SEQ ID NO: 3392)
EGFR-4811 19 nt Target #1: 5'-AGCACCGCUUUUGUUCUCG-3' (SEQ ID NO: 2873)
EGFR-4811 19 nt Target #2: 5'-UAGCACCGCUUUUGUUCUC-3' (SEQ ID NO: 3133)
EGFR-4811 19 nt Target #3: 5'-AUAGCACCGCUUUUGUUCU-3' (SEQ ID NO: 3393)

EGFR-4812 19 nt Target #1: 5'-GCACCGCUUUUGUUCUCGC-3' (SEQ ID NO: 2874)
 EGFR-4812 19 nt Target #2: 5'-AGCACCGCUUUUGUUCUCGC-3' (SEQ ID NO: 3134)
 EGFR-4812 19 nt Target #3: 5'-UAGCACCGCUUUUGUUCUC-3' (SEQ ID NO: 3394)
 EGFR-4813 19 nt Target #1: 5'-CACCGCUUUUGUUCUCGCA-3' (SEQ ID NO: 2875)
 EGFR-4813 19 nt Target #2: 5'-GCACCGCUUUUGUUCUCGC-3' (SEQ ID NO: 3135)
 EGFR-4813 19 nt Target #3: 5'-AGCACCGCUUUUGUUCUCGC-3' (SEQ ID NO: 3395)
 EGFR-4816 19 nt Target #1: 5'-CGCUUUUGUUCUCGCAAAA-3' (SEQ ID NO: 2876)
 EGFR-4816 19 nt Target #2: 5'-CCGCUUUUGUUCUCGCAAA-3' (SEQ ID NO: 3136)
 EGFR-4816 19 nt Target #3: 5'-ACCGCUUUUGUUCUCGCAA-3' (SEQ ID NO: 3396)
 EGFR-4817 19 nt Target #1: 5'-GCUUUUGUUCUCGCAAAAA-3' (SEQ ID NO: 2877)
 EGFR-4817 19 nt Target #2: 5'-CGCUUUUGUUCUCGCAAAA-3' (SEQ ID NO: 3137)
 EGFR-4817 19 nt Target #3: 5'-CCGCUUUUGUUCUCGCAAA-3' (SEQ ID NO: 3397)
 EGFR-4818 19 nt Target #1: 5'-CUUUUGUUCUCGCAAAAAC-3' (SEQ ID NO: 2878)
 EGFR-4818 19 nt Target #2: 5'-GCUUUUGUUCUCGCAAAAA-3' (SEQ ID NO: 3138)
 EGFR-4818 19 nt Target #3: 5'-CGCUUUUGUUCUCGCAAAA-3' (SEQ ID NO: 3398)
 EGFR-4819 19 nt Target #1: 5'-UUUUGUUCUCGCAAAAACG-3' (SEQ ID NO: 2879)
 EGFR-4819 19 nt Target #2: 5'-CUUUUGUUCUCGCAAAAAC-3' (SEQ ID NO: 3139)
 EGFR-4819 19 nt Target #3: 5'-GCUUUUGUUCUCGCAAAAAC-3' (SEQ ID NO: 3399)
 EGFR-4824 19 nt Target #1: 5'-UUCUCGCAAAAACGUAUCU-3' (SEQ ID NO: 2880)
 EGFR-4824 19 nt Target #2: 5'-GUUCUCGCAAAAACGUAUC-3' (SEQ ID NO: 3140)
 EGFR-4824 19 nt Target #3: 5'-UGUUCUCGCAAAAACGUAU-3' (SEQ ID NO: 3400)
 EGFR-4953 19 nt Target #1: 5'-AAAAUAGUUUGUGUUACUU-3' (SEQ ID NO: 2881)
 EGFR-4953 19 nt Target #2: 5'-AAAAUAGUUUGUGUUACU-3' (SEQ ID NO: 3141)
 EGFR-4953 19 nt Target #3: 5'-CAAAAUAGUUUGUGUUAC-3' (SEQ ID NO: 3401)
 EGFR-4970 19 nt Target #1: 5'-UUAUGGAAGAUAGUUUUCU-3' (SEQ ID NO: 2882)
 EGFR-4970 19 nt Target #2: 5'-CUUAUGGAAGAUAGUUUUC-3' (SEQ ID NO: 3142)
 EGFR-4970 19 nt Target #3: 5'-ACUUAUGGAAGAUAGUUUU-3' (SEQ ID NO: 3402)
 EGFR-5003 19 nt Target #1: 5'-UCAAAAGCUUUUUACUCA-3' (SEQ ID NO: 2883)
 EGFR-5003 19 nt Target #2: 5'-UUCAAAAGCUUUUUACUCA-3' (SEQ ID NO: 3143)
 EGFR-5003 19 nt Target #3: 5'-CUUCAAAAGCUUUUUACUC-3' (SEQ ID NO: 3403)
 EGFR-5206 19 nt Target #1: 5'-ACUAGGGUUUGAAAUUGAU-3' (SEQ ID NO: 2884)
 EGFR-5206 19 nt Target #2: 5'-AACUAGGGUUUGAAAUUGA-3' (SEQ ID NO: 3144)
 EGFR-5206 19 nt Target #3: 5'-AAACUAGGGUUUGAAAUUG-3' (SEQ ID NO: 3404)
 EGFR-5275 19 nt Target #1: 5'-UAAAAUAAUUCUCUACAA-3' (SEQ ID NO: 2885)
 EGFR-5275 19 nt Target #2: 5'-CUAAAAUAAUUCUCUACA-3' (SEQ ID NO: 3145)
 EGFR-5275 19 nt Target #3: 5'-CCUAAAAUAAUUCUCUAC-3' (SEQ ID NO: 3405)
 EGFR-5374 19 nt Target #1: 5'-CAGCAGUCCUUUGUAAACA-3' (SEQ ID NO: 2886)
 EGFR-5374 19 nt Target #2: 5'-ACAGCAGUCCUUUGUAAAC-3' (SEQ ID NO: 3146)
 EGFR-5374 19 nt Target #3: 5'-AACAGCAGUCCUUUGUAAA-3' (SEQ ID NO: 3406)
 EGFR-5429 19 nt Target #1: 5'-CAAUUUAUCAAGGAAGAAA-3' (SEQ ID NO: 2887)
 EGFR-5429 19 nt Target #2: 5'-CCAAUUUAUCAAGGAAGAA-3' (SEQ ID NO: 3147)
 EGFR-5429 19 nt Target #3: 5'-UCCAAUUUAUCAAGGAAGA-3' (SEQ ID NO: 3407)
 EGFR-5497 19 nt Target #1: 5'-UACAAAAUGUCCUUUUGC-3' (SEQ ID NO: 2888)
 EGFR-5497 19 nt Target #2: 5'-AUACAAAAUGUCCUUUUG-3' (SEQ ID NO: 3148)
 EGFR-5497 19 nt Target #3: 5'-CAUACAAAAUGUCCUUUU-3' (SEQ ID NO: 3408)
 EGFR-5505 19 nt Target #1: 5'-GUUCCUUUUGCUUUUAAAAG-3' (SEQ ID NO: 2889)
 EGFR-5505 19 nt Target #2: 5'-UGUCCUUUUGCUUUUAAA-3' (SEQ ID NO: 3149)
 EGFR-5505 19 nt Target #3: 5'-AUGUCCUUUUGCUUUUAA-3' (SEQ ID NO: 3409)
 EGFR-5506 19 nt Target #1: 5'-UUCUUUUGCUUUUAAAAGU-3' (SEQ ID NO: 2890)
 EGFR-5506 19 nt Target #2: 5'-GUUCCUUUUGCUUUUAAAAG-3' (SEQ ID NO: 3150)
 EGFR-5506 19 nt Target #3: 5'-UGUCCUUUUGCUUUUAAA-3' (SEQ ID NO: 3410)
 EGFR-5512 19 nt Target #1: 5'-UUGCUUUUAAAAGUAAUUUU-3' (SEQ ID NO: 2891)
 EGFR-5512 19 nt Target #2: 5'-UUUGCUUUUAAAAGUAAUUU-3' (SEQ ID NO: 3151)
 EGFR-5512 19 nt Target #3: 5'-UUUUGCUUUUAAAAGUAAUU-3' (SEQ ID NO: 3411)
 EGFR-5565 19 nt Target #1: 5'-GUUAAGAAAGUAUUUGAUU-3' (SEQ ID NO: 2892)
 EGFR-5565 19 nt Target #2: 5'-UGUUAAGAAAGUAUUUGAU-3' (SEQ ID NO: 3152)
 EGFR-5565 19 nt Target #3: 5'-UUGUUAAGAAAGUAUUUGA-3' (SEQ ID NO: 3412)
 EGFR-463 19 nt Target #1: 5'-UUGGAAAUUACCUAUGUGC-3' (SEQ ID NO: 2893)
 EGFR-463 19 nt Target #2: 5'-UUUGGAAAUUACCUAUGUG-3' (SEQ ID NO: 3153)

EGFR-463 19 nt Target #3: 5'-AUUUGGAAAUACCUAUGU-3' (SEQ ID NO: 3413)
EGFR-464 19 nt Target #1: 5'-UGGAAAUACCUAUGUGCA-3' (SEQ ID NO: 2894)
EGFR-464 19 nt Target #2: 5'-UUGGAAAUACCUAUGUGC-3' (SEQ ID NO: 3154)
EGFR-464 19 nt Target #3: 5'-UUUGGAAAUACCUAUGUG-3' (SEQ ID NO: 3414)
EGFR-496 19 nt Target #1: 5'-CUUCCUUCUAAAAGACCA-3' (SEQ ID NO: 2895)
EGFR-496 19 nt Target #2: 5'-UCUUCUUCUAAAAGACC-3' (SEQ ID NO: 3155)
EGFR-496 19 nt Target #3: 5'-AUCUUCUUCUAAAAGAC-3' (SEQ ID NO: 3415)
EGFR-497 19 nt Target #1: 5'-UUUCCUUCUAAAAGACCAU-3' (SEQ ID NO: 2896)
EGFR-497 19 nt Target #2: 5'-CUUCCUUCUAAAAGACCA-3' (SEQ ID NO: 3156)
EGFR-497 19 nt Target #3: 5'-UCUUCUUCUAAAAGACC-3' (SEQ ID NO: 3416)
EGFR-498 19 nt Target #1: 5'-UCCUUCUAAAAGACCAUC-3' (SEQ ID NO: 2897)
EGFR-498 19 nt Target #2: 5'-UUUCCUUCUAAAAGACCAU-3' (SEQ ID NO: 3157)
EGFR-498 19 nt Target #3: 5'-CUUCCUUCUAAAAGACCA-3' (SEQ ID NO: 3417)
EGFR-499 19 nt Target #1: 5'-UCCUUCUAAAAGACCAUCC-3' (SEQ ID NO: 2898)
EGFR-499 19 nt Target #2: 5'-UCCUUCUAAAAGACCAUC-3' (SEQ ID NO: 3158)
EGFR-499 19 nt Target #3: 5'-UUUCCUUCUAAAAGACCAU-3' (SEQ ID NO: 3418)
EGFR-500 19 nt Target #1: 5'-CCUUCUAAAAGACCAUCCA-3' (SEQ ID NO: 2899)
EGFR-500 19 nt Target #2: 5'-UCCUUCUAAAAGACCAUCC-3' (SEQ ID NO: 3159)
EGFR-500 19 nt Target #3: 5'-UCCUUCUAAAAGACCAUC-3' (SEQ ID NO: 3419)
EGFR-501 19 nt Target #1: 5'-CUUCUAAAAGACCAUCCAG-3' (SEQ ID NO: 2900)
EGFR-501 19 nt Target #2: 5'-CCUUCUAAAAGACCAUCCA-3' (SEQ ID NO: 3160)
EGFR-501 19 nt Target #3: 5'-UCCUUCUAAAAGACCAUCC-3' (SEQ ID NO: 3420)
EGFR-502 19 nt Target #1: 5'-UUCUAAAAGACCAUCCAGG-3' (SEQ ID NO: 2901)
EGFR-502 19 nt Target #2: 5'-CUUCUAAAAGACCAUCCAG-3' (SEQ ID NO: 3161)
EGFR-502 19 nt Target #3: 5'-CCUUCUAAAAGACCAUCCA-3' (SEQ ID NO: 3421)
EGFR-503 19 nt Target #1: 5'-UCUAAAAGACCAUCCAGGA-3' (SEQ ID NO: 2902)
EGFR-503 19 nt Target #2: 5'-UUCUAAAAGACCAUCCAGG-3' (SEQ ID NO: 3162)
EGFR-503 19 nt Target #3: 5'-CUUCUAAAAGACCAUCCAG-3' (SEQ ID NO: 3422)
EGFR-504 19 nt Target #1: 5'-CUUAAAAGACCAUCCAGGAG-3' (SEQ ID NO: 2903)
EGFR-504 19 nt Target #2: 5'-UCUAAAAGACCAUCCAGGA-3' (SEQ ID NO: 3163)
EGFR-504 19 nt Target #3: 5'-UUCUAAAAGACCAUCCAGG-3' (SEQ ID NO: 3423)
EGFR-505 19 nt Target #1: 5'-UUAAGACCAUCCAGGAGG-3' (SEQ ID NO: 2904)
EGFR-505 19 nt Target #2: 5'-CUUAAAAGACCAUCCAGGAG-3' (SEQ ID NO: 3164)
EGFR-505 19 nt Target #3: 5'-UCUAAAAGACCAUCCAGGA-3' (SEQ ID NO: 3424)
EGFR-506 19 nt Target #1: 5'-UAAAGACCAUCCAGGAGGU-3' (SEQ ID NO: 2905)
EGFR-506 19 nt Target #2: 5'-UUAAGACCAUCCAGGAGG-3' (SEQ ID NO: 3165)
EGFR-506 19 nt Target #3: 5'-CUUAAAAGACCAUCCAGGAG-3' (SEQ ID NO: 3425)
EGFR-507 19 nt Target #1: 5'-AAAGACCAUCCAGGAGGUG-3' (SEQ ID NO: 2906)
EGFR-507 19 nt Target #2: 5'-UAAAGACCAUCCAGGAGGU-3' (SEQ ID NO: 3166)
EGFR-507 19 nt Target #3: 5'-UUAAGACCAUCCAGGAGG-3' (SEQ ID NO: 3426)
EGFR-508 19 nt Target #1: 5'-AAGACCAUCCAGGAGGUGG-3' (SEQ ID NO: 2907)
EGFR-508 19 nt Target #2: 5'-AAAGACCAUCCAGGAGGUG-3' (SEQ ID NO: 3167)
EGFR-508 19 nt Target #3: 5'-UAAAGACCAUCCAGGAGGU-3' (SEQ ID NO: 3427)
EGFR-509 19 nt Target #1: 5'-AGACCAUCCAGGAGGUGGC-3' (SEQ ID NO: 2908)
EGFR-509 19 nt Target #2: 5'-AAGACCAUCCAGGAGGUGG-3' (SEQ ID NO: 3168)
EGFR-509 19 nt Target #3: 5'-AAAGACCAUCCAGGAGGUG-3' (SEQ ID NO: 3428)
EGFR-838 19 nt Target #1: 5'-UGUGAUCCAAGCUGUCCCA-3' (SEQ ID NO: 2909)
EGFR-838 19 nt Target #2: 5'-GUGUGAUCCAAGCUGUCCC-3' (SEQ ID NO: 3169)
EGFR-838 19 nt Target #3: 5'-AGUGUGAUCCAAGCUGUCC-3' (SEQ ID NO: 3429)
EGFR-839 19 nt Target #1: 5'-GUGAUCCAAGCUGUCCCAA-3' (SEQ ID NO: 2910)
EGFR-839 19 nt Target #2: 5'-UGUGAUCCAAGCUGUCCCA-3' (SEQ ID NO: 3170)
EGFR-839 19 nt Target #3: 5'-GUGUGAUCCAAGCUGUCCC-3' (SEQ ID NO: 3430)
EGFR-840 19 nt Target #1: 5'-UGAUCCAAGCUGUCCCAAU-3' (SEQ ID NO: 2911)
EGFR-840 19 nt Target #2: 5'-GUGAUCCAAGCUGUCCCAA-3' (SEQ ID NO: 3171)
EGFR-840 19 nt Target #3: 5'-UGUGAUCCAAGCUGUCCCA-3' (SEQ ID NO: 3431)
EGFR-841 19 nt Target #1: 5'-GAUCCAAGCUGUCCCAAUG-3' (SEQ ID NO: 2912)
EGFR-841 19 nt Target #2: 5'-UGAUCCAAGCUGUCCCAAU-3' (SEQ ID NO: 3172)
EGFR-841 19 nt Target #3: 5'-GUGAUCCAAGCUGUCCCAA-3' (SEQ ID NO: 3432)
EGFR-842 19 nt Target #1: 5'-AUCCAAGCUGUCCCAAUGG-3' (SEQ ID NO: 2913)

EGFR-842 19 nt Target #2: 5'-GAUCCAAGCUGUCCCAAUG-3' (SEQ ID NO: 3173)
EGFR-842 19 nt Target #3: 5'-UGAUCCAAGCUGUCCCAAU-3' (SEQ ID NO: 3433)
EGFR-876 19 nt Target #1: 5'-AGGAGAGGAGAACUGCCAG-3' (SEQ ID NO: 2914)
EGFR-876 19 nt Target #2: 5'-CAGGAGAGGAGAACUGCCA-3' (SEQ ID NO: 3174)
EGFR-876 19 nt Target #3: 5'-GCAGGAGAGGAGAACUGCC-3' (SEQ ID NO: 3434)
EGFR-877 19 nt Target #1: 5'-GGAGAGGAGAACUGCCAGA-3' (SEQ ID NO: 2915)
EGFR-877 19 nt Target #2: 5'-AGGAGAGGAGAACUGCCAG-3' (SEQ ID NO: 3175)
EGFR-877 19 nt Target #3: 5'-CAGGAGAGGAGAACUGCCA-3' (SEQ ID NO: 3435)
EGFR-878 19 nt Target #1: 5'-GAGAGGAGAACUGCCAGAA-3' (SEQ ID NO: 2916)
EGFR-878 19 nt Target #2: 5'-GGAGAGGAGAACUGCCAGA-3' (SEQ ID NO: 3176)
EGFR-878 19 nt Target #3: 5'-AGGAGAGGAGAACUGCCAG-3' (SEQ ID NO: 3436)
EGFR-879 19 nt Target #1: 5'-AGAGGAGAACUGCCAGAAA-3' (SEQ ID NO: 2917)
EGFR-879 19 nt Target #2: 5'-GAGAGGAGAACUGCCAGAA-3' (SEQ ID NO: 3177)
EGFR-879 19 nt Target #3: 5'-GGAGAGGAGAACUGCCAGA-3' (SEQ ID NO: 3437)
EGFR-899 19 nt Target #1: 5'-UGACCAAAAUCAUCUGUGC-3' (SEQ ID NO: 2918)
EGFR-899 19 nt Target #2: 5'-CUGACCAAAAUCAUCUGUG-3' (SEQ ID NO: 3178)
EGFR-899 19 nt Target #3: 5'-ACUGACCAAAAUCAUCUGU-3' (SEQ ID NO: 3438)
EGFR-900 19 nt Target #1: 5'-GACCAAAAUCAUCUGUGCC-3' (SEQ ID NO: 2919)
EGFR-900 19 nt Target #2: 5'-UGACCAAAAUCAUCUGUGC-3' (SEQ ID NO: 3179)
EGFR-900 19 nt Target #3: 5'-CUGACCAAAAUCAUCUGUG-3' (SEQ ID NO: 3439)
EGFR-901 19 nt Target #1: 5'-ACCAAAAUCAUCUGUGCCC-3' (SEQ ID NO: 2920)
EGFR-901 19 nt Target #2: 5'-GACCAAAAUCAUCUGUGCC-3' (SEQ ID NO: 3180)
EGFR-901 19 nt Target #3: 5'-UGACCAAAAUCAUCUGUGC-3' (SEQ ID NO: 3440)
EGFR-902 19 nt Target #1: 5'-CCAAAAUCAUCUGUGCCCA-3' (SEQ ID NO: 2921)
EGFR-902 19 nt Target #2: 5'-ACCAAAAUCAUCUGUGCCC-3' (SEQ ID NO: 3181)
EGFR-902 19 nt Target #3: 5'-GACCAAAAUCAUCUGUGCC-3' (SEQ ID NO: 3441)
EGFR-903 19 nt Target #1: 5'-CAAAAUCAUCUGUGCCCAG-3' (SEQ ID NO: 2922)
EGFR-903 19 nt Target #2: 5'-CCAAAAUCAUCUGUGCCCA-3' (SEQ ID NO: 3182)
EGFR-903 19 nt Target #3: 5'-ACCAAAAUCAUCUGUGCCC-3' (SEQ ID NO: 3442)
EGFR-904 19 nt Target #1: 5'-AAAAUCAUCUGUGCCCAGC-3' (SEQ ID NO: 2923)
EGFR-904 19 nt Target #2: 5'-CAAAAUCAUCUGUGCCCAG-3' (SEQ ID NO: 3183)
EGFR-904 19 nt Target #3: 5'-CCAAAAUCAUCUGUGCCCA-3' (SEQ ID NO: 3443)
EGFR-905 19 nt Target #1: 5'-AAAUCAUCUGUGCCCAGCA-3' (SEQ ID NO: 2924)
EGFR-905 19 nt Target #2: 5'-AAAAUCAUCUGUGCCCAGC-3' (SEQ ID NO: 3184)
EGFR-905 19 nt Target #3: 5'-CAAAAUCAUCUGUGCCCAG-3' (SEQ ID NO: 3444)
EGFR-954 19 nt Target #1: 5'-CAGUGACUGCUGCCACAAC-3' (SEQ ID NO: 2925)
EGFR-954 19 nt Target #2: 5'-CCAGUGACUGCUGCCACAA-3' (SEQ ID NO: 3185)
EGFR-954 19 nt Target #3: 5'-CCCAGUGACUGCUGCCACA-3' (SEQ ID NO: 3445)
EGFR-955 19 nt Target #1: 5'-AGUGACUGCUGCCACAACC-3' (SEQ ID NO: 2926)
EGFR-955 19 nt Target #2: 5'-CAGUGACUGCUGCCACAAC-3' (SEQ ID NO: 3186)
EGFR-955 19 nt Target #3: 5'-CCAGUGACUGCUGCCACAA-3' (SEQ ID NO: 3446)
EGFR-956 19 nt Target #1: 5'-GUGACUGCUGCCACAACCA-3' (SEQ ID NO: 2927)
EGFR-956 19 nt Target #2: 5'-AGUGACUGCUGCCACAACC-3' (SEQ ID NO: 3187)
EGFR-956 19 nt Target #3: 5'-CAGUGACUGCUGCCACAAC-3' (SEQ ID NO: 3447)
EGFR-1313 19 nt Target #1: 5'-CACUCUCCAUAUAAUAGCUAC-3' (SEQ ID NO: 2928)
EGFR-1313 19 nt Target #2: 5'-UCACUCUCCAUAUAAUAGCUA-3' (SEQ ID NO: 3188)
EGFR-1313 19 nt Target #3: 5'-CUCACUCUCCAUAUAAUAGCU-3' (SEQ ID NO: 3448)
EGFR-1480 19 nt Target #1: 5'-UUUUUGCUGAUUCAGGCUU-3' (SEQ ID NO: 2929)
EGFR-1480 19 nt Target #2: 5'-GUUUUUGCUGAUUCAGGCU-3' (SEQ ID NO: 3189)
EGFR-1480 19 nt Target #3: 5'-GGUUUUUGCUGAUUCAGGC-3' (SEQ ID NO: 3449)
EGFR-1481 19 nt Target #1: 5'-UUUUGCUGAUUCAGGCUUG-3' (SEQ ID NO: 2930)
EGFR-1481 19 nt Target #2: 5'-UUUUUGCUGAUUCAGGCUU-3' (SEQ ID NO: 3190)
EGFR-1481 19 nt Target #3: 5'-GUUUUUGCUGAUUCAGGCU-3' (SEQ ID NO: 3450)
EGFR-1482 19 nt Target #1: 5'-UUUGCUGAUUCAGGCUUGG-3' (SEQ ID NO: 2931)
EGFR-1482 19 nt Target #2: 5'-UUUUGCUGAUUCAGGCUUG-3' (SEQ ID NO: 3191)
EGFR-1482 19 nt Target #3: 5'-UUUUUGCUGAUUCAGGCUU-3' (SEQ ID NO: 3451)
EGFR-1483 19 nt Target #1: 5'-UUGCUGAUUCAGGCUUUGG-3' (SEQ ID NO: 2932)
EGFR-1483 19 nt Target #2: 5'-UUUGCUGAUUCAGGCUUGG-3' (SEQ ID NO: 3192)
EGFR-1483 19 nt Target #3: 5'-UUUUGCUGAUUCAGGCUUG-3' (SEQ ID NO: 3452)

EGFR-1484 19 nt Target #1: 5'-UGCUGAUUCAGGCUUGGCC-3' (SEQ ID NO: 2933)
EGFR-1484 19 nt Target #2: 5'-UUGCUGAUUCAGGCUUGGC-3' (SEQ ID NO: 3193)
EGFR-1484 19 nt Target #3: 5'-UUUGCUGAUUCAGGCUUGG-3' (SEQ ID NO: 3453)
EGFR-1485 19 nt Target #1: 5'-GCUGAUUCAGGCUUGGCCU-3' (SEQ ID NO: 2934)
EGFR-1485 19 nt Target #2: 5'-UGCUGAUUCAGGCUUGGCC-3' (SEQ ID NO: 3194)
EGFR-1485 19 nt Target #3: 5'-UUGCUGAUUCAGGCUUGGC-3' (SEQ ID NO: 3454)
EGFR-1486 19 nt Target #1: 5'-CUGAUUCAGGCUUGGCCUG-3' (SEQ ID NO: 2935)
EGFR-1486 19 nt Target #2: 5'-GCUGAUUCAGGCUUGGCCU-3' (SEQ ID NO: 3195)
EGFR-1486 19 nt Target #3: 5'-UGCUGAUUCAGGCUUGGCC-3' (SEQ ID NO: 3455)
EGFR-1487 19 nt Target #1: 5'-UGAUUCAGGCUUGGCCUGA-3' (SEQ ID NO: 2936)
EGFR-1487 19 nt Target #2: 5'-CUGAUUCAGGCUUGGCCUG-3' (SEQ ID NO: 3196)
EGFR-1487 19 nt Target #3: 5'-GCUGAUUCAGGCUUGGCCU-3' (SEQ ID NO: 3456)
EGFR-1561 19 nt Target #1: 5'-AAGCAACAUGGUCAGUUUU-3' (SEQ ID NO: 2937)
EGFR-1561 19 nt Target #2: 5'-CAAGCAACAUGGUCAGUUU-3' (SEQ ID NO: 3197)
EGFR-1561 19 nt Target #3: 5'-CCAAGCAACAUGGUCAGUU-3' (SEQ ID NO: 3457)
EGFR-1562 19 nt Target #1: 5'-AGCAACAUGGUCAGUUUUC-3' (SEQ ID NO: 2938)
EGFR-1562 19 nt Target #2: 5'-AAGCAACAUGGUCAGUUUU-3' (SEQ ID NO: 3198)
EGFR-1562 19 nt Target #3: 5'-CAAGCAACAUGGUCAGUUU-3' (SEQ ID NO: 3458)
EGFR-1563 19 nt Target #1: 5'-GCAACAUGGUCAGUUUUCU-3' (SEQ ID NO: 2939)
EGFR-1563 19 nt Target #2: 5'-AGCAACAUGGUCAGUUUUC-3' (SEQ ID NO: 3199)
EGFR-1563 19 nt Target #3: 5'-AAGCAACAUGGUCAGUUUU-3' (SEQ ID NO: 3459)
EGFR-1691 19 nt Target #1: 5'-CAAAUAAACUGGAAAAAACU-3' (SEQ ID NO: 2940)
EGFR-1691 19 nt Target #2: 5'-ACAAUAAACUGGAAAAAAC-3' (SEQ ID NO: 3200)
EGFR-1691 19 nt Target #3: 5'-UACAAUAAACUGGAAAAAA-3' (SEQ ID NO: 3460)
EGFR-1963 19 nt Target #1: 5'-CAGGCCAUGAACAUACC-3' (SEQ ID NO: 2941)
EGFR-1963 19 nt Target #2: 5'-UCAGGCCAUGAACAUACC-3' (SEQ ID NO: 3201)
EGFR-1963 19 nt Target #3: 5'-CUCAGGCCAUGAACAUAC-3' (SEQ ID NO: 3461)
EGFR-1964 19 nt Target #1: 5'-AGGCCAUGAACAUACCUG-3' (SEQ ID NO: 2942)
EGFR-1964 19 nt Target #2: 5'-CAGGCCAUGAACAUACC-3' (SEQ ID NO: 3202)
EGFR-1964 19 nt Target #3: 5'-UCAGGCCAUGAACAUACC-3' (SEQ ID NO: 3462)
EGFR-2008 19 nt Target #1: 5'-AUCCAGUGUGCCCACUACA-3' (SEQ ID NO: 2943)
EGFR-2008 19 nt Target #2: 5'-UAUCCAGUGUGCCCACUAC-3' (SEQ ID NO: 3203)
EGFR-2008 19 nt Target #3: 5'-GUAUCCAGUGUGCCCACUA-3' (SEQ ID NO: 3463)
EGFR-2009 19 nt Target #1: 5'-UCCAGUGUGCCCACUACAU-3' (SEQ ID NO: 2944)
EGFR-2009 19 nt Target #2: 5'-AUCCAGUGUGCCCACUACA-3' (SEQ ID NO: 3204)
EGFR-2009 19 nt Target #3: 5'-UAUCCAGUGUGCCCACUAC-3' (SEQ ID NO: 3464)
EGFR-2010 19 nt Target #1: 5'-CCAGUGUGCCCACUACAUU-3' (SEQ ID NO: 2945)
EGFR-2010 19 nt Target #2: 5'-UCCAGUGUGCCCACUACAU-3' (SEQ ID NO: 3205)
EGFR-2010 19 nt Target #3: 5'-AUCCAGUGUGCCCACUACA-3' (SEQ ID NO: 3465)
EGFR-2011 19 nt Target #1: 5'-CAGUGUGCCCACUACAUUG-3' (SEQ ID NO: 2946)
EGFR-2011 19 nt Target #2: 5'-CCAGUGUGCCCACUACAUU-3' (SEQ ID NO: 3206)
EGFR-2011 19 nt Target #3: 5'-UCCAGUGUGCCCACUACAU-3' (SEQ ID NO: 3466)
EGFR-2012 19 nt Target #1: 5'-AGUGUGCCCACUACAUUGA-3' (SEQ ID NO: 2947)
EGFR-2012 19 nt Target #2: 5'-CAGUGUGCCCACUACAUUG-3' (SEQ ID NO: 3207)
EGFR-2012 19 nt Target #3: 5'-CCAGUGUGCCCACUACAUU-3' (SEQ ID NO: 3467)
EGFR-2401 19 nt Target #1: 5'-GAAUUCAAAAAGAUCAAAG-3' (SEQ ID NO: 2948)
EGFR-2401 19 nt Target #2: 5'-UGAAUUCAAAAAGAUCAAA-3' (SEQ ID NO: 3208)
EGFR-2401 19 nt Target #3: 5'-CUGAAUUCAAAAAGAUCAA-3' (SEQ ID NO: 3468)
EGFR-2402 19 nt Target #1: 5'-AAUUCAAAAAGAUCAAAGU-3' (SEQ ID NO: 2949)
EGFR-2402 19 nt Target #2: 5'-GAAUUCAAAAAGAUCAAAG-3' (SEQ ID NO: 3209)
EGFR-2402 19 nt Target #3: 5'-UGAAUUCAAAAAGAUCAAA-3' (SEQ ID NO: 3469)
EGFR-2458 19 nt Target #1: 5'-CUCUGGAUCCCAGAAGGUG-3' (SEQ ID NO: 2950)
EGFR-2458 19 nt Target #2: 5'-ACUCUGGAUCCCAGAAGGU-3' (SEQ ID NO: 3210)
EGFR-2458 19 nt Target #3: 5'-GACUCUGGAUCCCAGAAGG-3' (SEQ ID NO: 3470)
EGFR-2459 19 nt Target #1: 5'-UCUGGAUCCCAGAAGGUGA-3' (SEQ ID NO: 2951)
EGFR-2459 19 nt Target #2: 5'-CUCUGGAUCCCAGAAGGUG-3' (SEQ ID NO: 3211)
EGFR-2459 19 nt Target #3: 5'-ACUCUGGAUCCCAGAAGGU-3' (SEQ ID NO: 3471)
EGFR-2460 19 nt Target #1: 5'-CUGGAUCCCAGAAGGUGAG-3' (SEQ ID NO: 2952)
EGFR-2460 19 nt Target #2: 5'-UCUGGAUCCCAGAAGGUGA-3' (SEQ ID NO: 3212)

EGFR-2460 19 nt Target #3: 5'-CUCUGGAUCCCAGAAGGUG-3' (SEQ ID NO: 3472)
EGFR-2461 19 nt Target #1: 5'-UGGAUCCCAGAAGGUGAGA-3' (SEQ ID NO: 2953)
EGFR-2461 19 nt Target #2: 5'-CUGGAUCCCAGAAGGUGAG-3' (SEQ ID NO: 3213)
EGFR-2461 19 nt Target #3: 5'-UCUGGAUCCCAGAAGGUGA-3' (SEQ ID NO: 3473)
EGFR-2462 19 nt Target #1: 5'-GGAUCCCAGAAGGUGAGAA-3' (SEQ ID NO: 2954)
EGFR-2462 19 nt Target #2: 5'-UGGAUCCCAGAAGGUGAGA-3' (SEQ ID NO: 3214)
EGFR-2462 19 nt Target #3: 5'-CUGGAUCCCAGAAGGUGAG-3' (SEQ ID NO: 3474)
EGFR-2463 19 nt Target #1: 5'-GAUCCCAGAAGGUGAGAAA-3' (SEQ ID NO: 2955)
EGFR-2463 19 nt Target #2: 5'-GGAUCCCAGAAGGUGAGAA-3' (SEQ ID NO: 3215)
EGFR-2463 19 nt Target #3: 5'-UGGAUCCCAGAAGGUGAGA-3' (SEQ ID NO: 3475)
EGFR-2464 19 nt Target #1: 5'-AUCCCAGAAGGUGAGAAAAG-3' (SEQ ID NO: 2956)
EGFR-2464 19 nt Target #2: 5'-GAUCCCAGAAGGUGAGAAA-3' (SEQ ID NO: 3216)
EGFR-2464 19 nt Target #3: 5'-GGAUCCCAGAAGGUGAGAA-3' (SEQ ID NO: 3476)
EGFR-2465 19 nt Target #1: 5'-UCCCAGAAGGUGAGAAAGU-3' (SEQ ID NO: 2957)
EGFR-2465 19 nt Target #2: 5'-AUCCCAGAAGGUGAGAAAAG-3' (SEQ ID NO: 3217)
EGFR-2465 19 nt Target #3: 5'-GAUCCCAGAAGGUGAGAAA-3' (SEQ ID NO: 3477)
EGFR-2815 19 nt Target #1: 5'-CAGCAUGUCAAGAUACACAG-3' (SEQ ID NO: 2958)
EGFR-2815 19 nt Target #2: 5'-GCAGCAUGUCAAGAUACACA-3' (SEQ ID NO: 3218)
EGFR-2815 19 nt Target #3: 5'-CGCAGCAUGUCAAGAUACAC-3' (SEQ ID NO: 3478)
EGFR-2816 19 nt Target #1: 5'-AGCAUGUCAAGAUACACAGA-3' (SEQ ID NO: 2959)
EGFR-2816 19 nt Target #2: 5'-CAGCAUGUCAAGAUACACAG-3' (SEQ ID NO: 3219)
EGFR-2816 19 nt Target #3: 5'-GCAGCAUGUCAAGAUACACA-3' (SEQ ID NO: 3479)
EGFR-2817 19 nt Target #1: 5'-GCAUGUCAAGAUACACAGAU-3' (SEQ ID NO: 2960)
EGFR-2817 19 nt Target #2: 5'-AGCAUGUCAAGAUACACAGA-3' (SEQ ID NO: 3220)
EGFR-2817 19 nt Target #3: 5'-CAGCAUGUCAAGAUACACAG-3' (SEQ ID NO: 3480)
EGFR-2818 19 nt Target #1: 5'-CAUGUCAAGAUACACAGAUU-3' (SEQ ID NO: 2961)
EGFR-2818 19 nt Target #2: 5'-GCAUGUCAAGAUACACAGAU-3' (SEQ ID NO: 3221)
EGFR-2818 19 nt Target #3: 5'-AGCAUGUCAAGAUACACAGA-3' (SEQ ID NO: 3481)
EGFR-2819 19 nt Target #1: 5'-AUGUCAAGAUACACAGAUUU-3' (SEQ ID NO: 2962)
EGFR-2819 19 nt Target #2: 5'-CAUGUCAAGAUACACAGAUU-3' (SEQ ID NO: 3222)
EGFR-2819 19 nt Target #3: 5'-GCAUGUCAAGAUACACAGAU-3' (SEQ ID NO: 3482)
EGFR-2820 19 nt Target #1: 5'-UGUCAAGAUACACAGAUUUU-3' (SEQ ID NO: 2963)
EGFR-2820 19 nt Target #2: 5'-AUGUCAAGAUACACAGAUUU-3' (SEQ ID NO: 3223)
EGFR-2820 19 nt Target #3: 5'-CAUGUCAAGAUACACAGAUU-3' (SEQ ID NO: 3483)
EGFR-2821 19 nt Target #1: 5'-GUCAAGAUACACAGAUUUUG-3' (SEQ ID NO: 2964)
EGFR-2821 19 nt Target #2: 5'-UGUCAAGAUACACAGAUUUU-3' (SEQ ID NO: 3224)
EGFR-2821 19 nt Target #3: 5'-AUGUCAAGAUACACAGAUUU-3' (SEQ ID NO: 3484)
EGFR-2822 19 nt Target #1: 5'-UCAAGAUACACAGAUUUUGG-3' (SEQ ID NO: 2965)
EGFR-2822 19 nt Target #2: 5'-GUCAAGAUACACAGAUUUUG-3' (SEQ ID NO: 3225)
EGFR-2822 19 nt Target #3: 5'-UGUCAAGAUACACAGAUUUU-3' (SEQ ID NO: 3485)
EGFR-2823 19 nt Target #1: 5'-CAAGAUACACAGAUUUUGGG-3' (SEQ ID NO: 2966)
EGFR-2823 19 nt Target #2: 5'-UCAAGAUACACAGAUUUUGG-3' (SEQ ID NO: 3226)
EGFR-2823 19 nt Target #3: 5'-GUCAAGAUACACAGAUUUUG-3' (SEQ ID NO: 3486)
EGFR-2824 19 nt Target #1: 5'-AAGAUACACAGAUUUUGGGC-3' (SEQ ID NO: 2967)
EGFR-2824 19 nt Target #2: 5'-CAAGAUACACAGAUUUUGGG-3' (SEQ ID NO: 3227)
EGFR-2824 19 nt Target #3: 5'-UCAAGAUACACAGAUUUUGG-3' (SEQ ID NO: 3487)
EGFR-2825 19 nt Target #1: 5'-AGAUCACAGAUUUUGGGCU-3' (SEQ ID NO: 2968)
EGFR-2825 19 nt Target #2: 5'-AAGAUACACAGAUUUUGGGC-3' (SEQ ID NO: 3228)
EGFR-2825 19 nt Target #3: 5'-CAAGAUACACAGAUUUUGGG-3' (SEQ ID NO: 3488)
EGFR-2826 19 nt Target #1: 5'-GAUCACAGAUUUUGGGCUG-3' (SEQ ID NO: 2969)
EGFR-2826 19 nt Target #2: 5'-AGAUCACAGAUUUUGGGCU-3' (SEQ ID NO: 3229)
EGFR-2826 19 nt Target #3: 5'-AAGAUACACAGAUUUUGGGC-3' (SEQ ID NO: 3489)
EGFR-2827 19 nt Target #1: 5'-AUCACAGAUUUUGGGCUGG-3' (SEQ ID NO: 2970)
EGFR-2827 19 nt Target #2: 5'-GAUCACAGAUUUUGGGCUG-3' (SEQ ID NO: 3230)
EGFR-2827 19 nt Target #3: 5'-AGAUCACAGAUUUUGGGCU-3' (SEQ ID NO: 3490)
EGFR-2828 19 nt Target #1: 5'-UCACAGAUUUUGGGCUGGC-3' (SEQ ID NO: 2971)
EGFR-2828 19 nt Target #2: 5'-AUCACAGAUUUUGGGCUGG-3' (SEQ ID NO: 3231)
EGFR-2828 19 nt Target #3: 5'-GAUCACAGAUUUUGGGCUG-3' (SEQ ID NO: 3491)
EGFR-2829 19 nt Target #1: 5'-CACAGAUUUUGGGCUGGCC-3' (SEQ ID NO: 2972)

EGFR-2829 19 nt Target #2: 5'-UCACAGAUUUUGGGCUGGC-3' (SEQ ID NO: 3232)
EGFR-2829 19 nt Target #3: 5'-AUCACAGAUUUUGGGCUGG-3' (SEQ ID NO: 3492)
EGFR-2830 19 nt Target #1: 5'-ACAGAUUUUGGGCUGGCCA-3' (SEQ ID NO: 2973)
EGFR-2830 19 nt Target #2: 5'-CACAGAUUUUGGGCUGGCC-3' (SEQ ID NO: 3233)
EGFR-2830 19 nt Target #3: 5'-UCACAGAUUUUGGGCUGGC-3' (SEQ ID NO: 3493)
EGFR-2831 19 nt Target #1: 5'-CAGAUUUUGGGCUGGCCAA-3' (SEQ ID NO: 2974)
EGFR-2831 19 nt Target #2: 5'-ACAGAUUUUGGGCUGGCCA-3' (SEQ ID NO: 3234)
EGFR-2831 19 nt Target #3: 5'-CACAGAUUUUGGGCUGGCC-3' (SEQ ID NO: 3494)
EGFR-2832 19 nt Target #1: 5'-AGAUUUUGGGCUGGCCAAA-3' (SEQ ID NO: 2975)
EGFR-2832 19 nt Target #2: 5'-CAGAUUUUGGGCUGGCCAA-3' (SEQ ID NO: 3235)
EGFR-2832 19 nt Target #3: 5'-ACAGAUUUUGGGCUGGCCA-3' (SEQ ID NO: 3495)
EGFR-2833 19 nt Target #1: 5'-GAUUUUUGGGCUGGCCAAAC-3' (SEQ ID NO: 2976)
EGFR-2833 19 nt Target #2: 5'-AGAUUUUGGGCUGGCCAAA-3' (SEQ ID NO: 3236)
EGFR-2833 19 nt Target #3: 5'-CAGAUUUUGGGCUGGCCAA-3' (SEQ ID NO: 3496)
EGFR-2834 19 nt Target #1: 5'-AUUUUGGGCUGGCCAAACU-3' (SEQ ID NO: 2977)
EGFR-2834 19 nt Target #2: 5'-GAUUUUUGGGCUGGCCAAAC-3' (SEQ ID NO: 3237)
EGFR-2834 19 nt Target #3: 5'-AGAUUUUGGGCUGGCCAAA-3' (SEQ ID NO: 3497)
EGFR-2835 19 nt Target #1: 5'-UUUUGGGCUGGCCAAACUG-3' (SEQ ID NO: 2978)
EGFR-2835 19 nt Target #2: 5'-AUUUUGGGCUGGCCAAACU-3' (SEQ ID NO: 3238)
EGFR-2835 19 nt Target #3: 5'-GAUUUUUGGGCUGGCCAAAC-3' (SEQ ID NO: 3498)
EGFR-2836 19 nt Target #1: 5'-UUUUGGGCUGGCCAAACUGC-3' (SEQ ID NO: 2979)
EGFR-2836 19 nt Target #2: 5'-UUUUGGGCUGGCCAAACUG-3' (SEQ ID NO: 3239)
EGFR-2836 19 nt Target #3: 5'-AUUUUGGGCUGGCCAAACU-3' (SEQ ID NO: 3499)
EGFR-2837 19 nt Target #1: 5'-UUGGGCUGGCCAAACUGCU-3' (SEQ ID NO: 2980)
EGFR-2837 19 nt Target #2: 5'-UUUGGGCUGGCCAAACUGC-3' (SEQ ID NO: 3240)
EGFR-2837 19 nt Target #3: 5'-UUUUGGGCUGGCCAAACUG-3' (SEQ ID NO: 3500)
EGFR-2891 19 nt Target #1: 5'-GCAAAGUGCCUAUCAAGUG-3' (SEQ ID NO: 2981)
EGFR-2891 19 nt Target #2: 5'-GGCAAAGUGCCUAUCAAGU-3' (SEQ ID NO: 3241)
EGFR-2891 19 nt Target #3: 5'-AGGCAAAGUGCCUAUCAAG-3' (SEQ ID NO: 3501)
EGFR-2892 19 nt Target #1: 5'-CAAAGUGCCUAUCAAGUGG-3' (SEQ ID NO: 2982)
EGFR-2892 19 nt Target #2: 5'-GCAAAGUGCCUAUCAAGUG-3' (SEQ ID NO: 3242)
EGFR-2892 19 nt Target #3: 5'-GGCAAAGUGCCUAUCAAGU-3' (SEQ ID NO: 3502)
EGFR-2893 19 nt Target #1: 5'-AAAGUGCCUAUCAAGUGGA-3' (SEQ ID NO: 2983)
EGFR-2893 19 nt Target #2: 5'-CAAAGUGCCUAUCAAGUGG-3' (SEQ ID NO: 3243)
EGFR-2893 19 nt Target #3: 5'-GCAAAGUGCCUAUCAAGUG-3' (SEQ ID NO: 3503)
EGFR-2894 19 nt Target #1: 5'-AAGUGCCUAUCAAGUGGAU-3' (SEQ ID NO: 2984)
EGFR-2894 19 nt Target #2: 5'-AAAGUGCCUAUCAAGUGGA-3' (SEQ ID NO: 3244)
EGFR-2894 19 nt Target #3: 5'-CAAAGUGCCUAUCAAGUGG-3' (SEQ ID NO: 3504)
EGFR-2895 19 nt Target #1: 5'-AGUGCCUAUCAAGUGGAUG-3' (SEQ ID NO: 2985)
EGFR-2895 19 nt Target #2: 5'-AAGUGCCUAUCAAGUGGAU-3' (SEQ ID NO: 3245)
EGFR-2895 19 nt Target #3: 5'-AAAGUGCCUAUCAAGUGGA-3' (SEQ ID NO: 3505)
EGFR-2896 19 nt Target #1: 5'-GUGCCUAUCAAGUGGAUGG-3' (SEQ ID NO: 2986)
EGFR-2896 19 nt Target #2: 5'-AGUGCCUAUCAAGUGGAUG-3' (SEQ ID NO: 3246)
EGFR-2896 19 nt Target #3: 5'-AAGUGCCUAUCAAGUGGAU-3' (SEQ ID NO: 3506)
EGFR-2897 19 nt Target #1: 5'-UGCCUAUCAAGUGGAUGGC-3' (SEQ ID NO: 2987)
EGFR-2897 19 nt Target #2: 5'-GUGCCUAUCAAGUGGAUGG-3' (SEQ ID NO: 3247)
EGFR-2897 19 nt Target #3: 5'-AGUGCCUAUCAAGUGGAUG-3' (SEQ ID NO: 3507)
EGFR-3088 19 nt Target #1: 5'-ACCAUCGAUGUCUACAUGA-3' (SEQ ID NO: 2988)
EGFR-3088 19 nt Target #2: 5'-UACCAUCGAUGUCUACAUG-3' (SEQ ID NO: 3248)
EGFR-3088 19 nt Target #3: 5'-GUACCAUCGAUGUCUACAU-3' (SEQ ID NO: 3508)
EGFR-3089 19 nt Target #1: 5'-CCAUCGAUGUCUACAUGAU-3' (SEQ ID NO: 2989)
EGFR-3089 19 nt Target #2: 5'-ACCAUCGAUGUCUACAUGA-3' (SEQ ID NO: 3249)
EGFR-3089 19 nt Target #3: 5'-UACCAUCGAUGUCUACAUG-3' (SEQ ID NO: 3509)
EGFR-3090 19 nt Target #1: 5'-CAUCGAUGUCUACAUGAUC-3' (SEQ ID NO: 2990)
EGFR-3090 19 nt Target #2: 5'-CCAUCGAUGUCUACAUGAU-3' (SEQ ID NO: 3250)
EGFR-3090 19 nt Target #3: 5'-ACCAUCGAUGUCUACAUGA-3' (SEQ ID NO: 3510)
EGFR-3091 19 nt Target #1: 5'-AUCGAUGUCUACAUGAUCA-3' (SEQ ID NO: 2991)
EGFR-3091 19 nt Target #2: 5'-CAUCGAUGUCUACAUGAUC-3' (SEQ ID NO: 3251)
EGFR-3091 19 nt Target #3: 5'-CCAUCGAUGUCUACAUGAU-3' (SEQ ID NO: 3511)

EGFR-3092 19 nt Target #1: 5'-UCGAUGUCUACAUGAUC AU-3' (SEQ ID NO: 2992)
EGFR-3092 19 nt Target #2: 5'-AUCGAUGUCUACAUGAUC A-3' (SEQ ID NO: 3252)
EGFR-3092 19 nt Target #3: 5'-CAUCGAUGUCUACAUGAUC-3' (SEQ ID NO: 3512)
EGFR-3093 19 nt Target #1: 5'-CGAUGUCUACAUGAUC AU-3' (SEQ ID NO: 2993)
EGFR-3093 19 nt Target #2: 5'-UCGAUGUCUACAUGAUC AU-3' (SEQ ID NO: 3253)
EGFR-3093 19 nt Target #3: 5'-AUCGAUGUCUACAUGAUC A-3' (SEQ ID NO: 3513)
EGFR-3094 19 nt Target #1: 5'-GAUGUCUACAUGAUC AUGG-3' (SEQ ID NO: 2994)
EGFR-3094 19 nt Target #2: 5'-CGAUGUCUACAUGAUC AUG-3' (SEQ ID NO: 3254)
EGFR-3094 19 nt Target #3: 5'-UCGAUGUCUACAUGAUC AU-3' (SEQ ID NO: 3514)
EGFR-3095 19 nt Target #1: 5'-AUGUCUACAUGAUC AUGGU-3' (SEQ ID NO: 2995)
EGFR-3095 19 nt Target #2: 5'-GAUGUCUACAUGAUC AUGG-3' (SEQ ID NO: 3255)
EGFR-3095 19 nt Target #3: 5'-CGAUGUCUACAUGAUC AUG-3' (SEQ ID NO: 3515)
EGFR-3096 19 nt Target #1: 5'-UGUCUACAUGAUC AUGGUC-3' (SEQ ID NO: 2996)
EGFR-3096 19 nt Target #2: 5'-AUGUCUACAUGAUC AUGGU-3' (SEQ ID NO: 3256)
EGFR-3096 19 nt Target #3: 5'-GAUGUCUACAUGAUC AUGG-3' (SEQ ID NO: 3516)
EGFR-3097 19 nt Target #1: 5'-GUCUACAUGAUC AUGGUCA-3' (SEQ ID NO: 2997)
EGFR-3097 19 nt Target #2: 5'-UGUCUACAUGAUC AUGGUC-3' (SEQ ID NO: 3257)
EGFR-3097 19 nt Target #3: 5'-AUGUCUACAUGAUC AUGGU-3' (SEQ ID NO: 3517)
EGFR-3098 19 nt Target #1: 5'-UCUACAUGAUC AUGGUCAA-3' (SEQ ID NO: 2998)
EGFR-3098 19 nt Target #2: 5'-GUCUACAUGAUC AUGGUCA-3' (SEQ ID NO: 3258)
EGFR-3098 19 nt Target #3: 5'-UGUCUACAUGAUC AUGGUC-3' (SEQ ID NO: 3518)
EGFR-3099 19 nt Target #1: 5'-CUACAUGAUC AUGGUCAA-3' (SEQ ID NO: 2999)
EGFR-3099 19 nt Target #2: 5'-UCUACAUGAUC AUGGUCAA-3' (SEQ ID NO: 3259)
EGFR-3099 19 nt Target #3: 5'-GUCUACAUGAUC AUGGUCA-3' (SEQ ID NO: 3519)
EGFR-3100 19 nt Target #1: 5'-UACAUGAUC AUGGUCAA-3' (SEQ ID NO: 3000)
EGFR-3100 19 nt Target #2: 5'-CUACAUGAUC AUGGUCAA-3' (SEQ ID NO: 3260)
EGFR-3100 19 nt Target #3: 5'-UCUACAUGAUC AUGGUCAA-3' (SEQ ID NO: 3520)
EGFR-3101 19 nt Target #1: 5'-ACAUGAUC AUGGUCAA-3' (SEQ ID NO: 3001)
EGFR-3101 19 nt Target #2: 5'-UACAUGAUC AUGGUCAA-3' (SEQ ID NO: 3261)
EGFR-3101 19 nt Target #3: 5'-CUACAUGAUC AUGGUCAA-3' (SEQ ID NO: 3521)
EGFR-3102 19 nt Target #1: 5'-CAUGAUC AUGGUCAA-3' (SEQ ID NO: 3002)
EGFR-3102 19 nt Target #2: 5'-ACAUGAUC AUGGUCAA-3' (SEQ ID NO: 3262)
EGFR-3102 19 nt Target #3: 5'-UACAUGAUC AUGGUCAA-3' (SEQ ID NO: 3522)
EGFR-3103 19 nt Target #1: 5'-AUGAUC AUGGUCAA-3' (SEQ ID NO: 3003)
EGFR-3103 19 nt Target #2: 5'-CAUGAUC AUGGUCAA-3' (SEQ ID NO: 3263)
EGFR-3103 19 nt Target #3: 5'-ACAUGAUC AUGGUCAA-3' (SEQ ID NO: 3523)
EGFR-3104 19 nt Target #1: 5'-UGAUC AUGGUCAA-3' (SEQ ID NO: 3004)
EGFR-3104 19 nt Target #2: 5'-AUGAUC AUGGUCAA-3' (SEQ ID NO: 3264)
EGFR-3104 19 nt Target #3: 5'-CAUGAUC AUGGUCAA-3' (SEQ ID NO: 3524)
EGFR-3105 19 nt Target #1: 5'-GAUC AUGGUCAA-3' (SEQ ID NO: 3005)
EGFR-3105 19 nt Target #2: 5'-UGAUC AUGGUCAA-3' (SEQ ID NO: 3265)
EGFR-3105 19 nt Target #3: 5'-AUGAUC AUGGUCAA-3' (SEQ ID NO: 3525)
EGFR-3106 19 nt Target #1: 5'-AUCAUGGUCAA-3' (SEQ ID NO: 3006)
EGFR-3106 19 nt Target #2: 5'-GAUC AUGGUCAA-3' (SEQ ID NO: 3266)
EGFR-3106 19 nt Target #3: 5'-UGAUC AUGGUCAA-3' (SEQ ID NO: 3526)
EGFR-3107 19 nt Target #1: 5'-UCAUGGUCAA-3' (SEQ ID NO: 3007)
EGFR-3107 19 nt Target #2: 5'-AUCAUGGUCAA-3' (SEQ ID NO: 3267)
EGFR-3107 19 nt Target #3: 5'-GAUC AUGGUCAA-3' (SEQ ID NO: 3527)
EGFR-3108 19 nt Target #1: 5'-CAUGGUCAA-3' (SEQ ID NO: 3008)
EGFR-3108 19 nt Target #2: 5'-UCAUGGUCAA-3' (SEQ ID NO: 3268)
EGFR-3108 19 nt Target #3: 5'-AUCAUGGUCAA-3' (SEQ ID NO: 3528)
EGFR-3109 19 nt Target #1: 5'-AUGGUCAA-3' (SEQ ID NO: 3009)
EGFR-3109 19 nt Target #2: 5'-CAUGGUCAA-3' (SEQ ID NO: 3269)
EGFR-3109 19 nt Target #3: 5'-UCAUGGUCAA-3' (SEQ ID NO: 3529)
EGFR-3110 19 nt Target #1: 5'-UGGUCAA-3' (SEQ ID NO: 3010)
EGFR-3110 19 nt Target #2: 5'-AUGGUCAA-3' (SEQ ID NO: 3270)
EGFR-3110 19 nt Target #3: 5'-CAUGGUCAA-3' (SEQ ID NO: 3530)
EGFR-3111 19 nt Target #1: 5'-GGUCAA-3' (SEQ ID NO: 3011)
EGFR-3111 19 nt Target #2: 5'-UGGUCAA-3' (SEQ ID NO: 3271)

EGFR-3111 19 nt Target #3: 5'-AUGGUCAAGUGCUGGAUGA-3' (SEQ ID NO: 3531)
 EGFR-3112 19 nt Target #1: 5'-GUCAAGUGCUGGAUGAUAG-3' (SEQ ID NO: 3012)
 EGFR-3112 19 nt Target #2: 5'-GGUCAAGUGCUGGAUGAUA-3' (SEQ ID NO: 3272)
 EGFR-3112 19 nt Target #3: 5'-UGGUCAAGUGCUGGAUGAU-3' (SEQ ID NO: 3532)
 EGFR-3113 19 nt Target #1: 5'-UCAAGUGCUGGAUGAUAGA-3' (SEQ ID NO: 3013)
 EGFR-3113 19 nt Target #2: 5'-GUCAAGUGCUGGAUGAUAG-3' (SEQ ID NO: 3273)
 EGFR-3113 19 nt Target #3: 5'-GGUCAAGUGCUGGAUGAUA-3' (SEQ ID NO: 3533)
 EGFR-3169 19 nt Target #1: 5'-GAAUUCUCCAAAAUGGCC-3' (SEQ ID NO: 3014)
 EGFR-3169 19 nt Target #2: 5'-CGAAUUCUCCAAAAUGGCC-3' (SEQ ID NO: 3274)
 EGFR-3169 19 nt Target #3: 5'-UCGAAUUCUCCAAAAUGGCC-3' (SEQ ID NO: 3534)
 EGFR-3170 19 nt Target #1: 5'-AAUUCUCCAAAAUGGCCCG-3' (SEQ ID NO: 3015)
 EGFR-3170 19 nt Target #2: 5'-GAAUUCUCCAAAAUGGCC-3' (SEQ ID NO: 3275)
 EGFR-3170 19 nt Target #3: 5'-CGAAUUCUCCAAAAUGGCC-3' (SEQ ID NO: 3535)
 EGFR-3220 19 nt Target #1: 5'-GAUGAAAGAAUGCAUUUGC-3' (SEQ ID NO: 3016)
 EGFR-3220 19 nt Target #2: 5'-GGAUGAAAGAAUGCAUUUG-3' (SEQ ID NO: 3276)
 EGFR-3220 19 nt Target #3: 5'-GGGAUGAAAGAAUGCAUUU-3' (SEQ ID NO: 3536)
 EGFR-3221 19 nt Target #1: 5'-AUGAAAGAAUGCAUUUGCC-3' (SEQ ID NO: 3017)
 EGFR-3221 19 nt Target #2: 5'-GAUGAAAGAAUGCAUUUGC-3' (SEQ ID NO: 3277)
 EGFR-3221 19 nt Target #3: 5'-GGAUGAAAGAAUGCAUUUG-3' (SEQ ID NO: 3537)
 EGFR-3222 19 nt Target #1: 5'-UGAAAGAAUGCAUUUGCCA-3' (SEQ ID NO: 3018)
 EGFR-3222 19 nt Target #2: 5'-AUGAAAGAAUGCAUUUGCC-3' (SEQ ID NO: 3278)
 EGFR-3222 19 nt Target #3: 5'-GAUGAAAGAAUGCAUUUGC-3' (SEQ ID NO: 3538)
 EGFR-3223 19 nt Target #1: 5'-GAAAGAAUGCAUUUGCCAA-3' (SEQ ID NO: 3019)
 EGFR-3223 19 nt Target #2: 5'-UGAAAGAAUGCAUUUGCCA-3' (SEQ ID NO: 3279)
 EGFR-3223 19 nt Target #3: 5'-AUGAAAGAAUGCAUUUGCC-3' (SEQ ID NO: 3539)
 EGFR-3224 19 nt Target #1: 5'-AAAGAAUGCAUUUGCCAAG-3' (SEQ ID NO: 3020)
 EGFR-3224 19 nt Target #2: 5'-GAAAGAAUGCAUUUGCCAA-3' (SEQ ID NO: 3280)
 EGFR-3224 19 nt Target #3: 5'-UGAAAGAAUGCAUUUGCCA-3' (SEQ ID NO: 3540)
 EGFR-3772 19 nt Target #1: 5'-GACAACCCUGACUACCAGC-3' (SEQ ID NO: 3021)
 EGFR-3772 19 nt Target #2: 5'-GGACAACCCUGACUACCAG-3' (SEQ ID NO: 3281)
 EGFR-3772 19 nt Target #3: 5'-UGGACAACCCUGACUACCA-3' (SEQ ID NO: 3541)
 EGFR-3773 19 nt Target #1: 5'-ACAACCCUGACUACCAGCA-3' (SEQ ID NO: 3022)
 EGFR-3773 19 nt Target #2: 5'-GACAACCCUGACUACCAGC-3' (SEQ ID NO: 3282)
 EGFR-3773 19 nt Target #3: 5'-GGACAACCCUGACUACCAG-3' (SEQ ID NO: 3542)
 EGFR-3774 19 nt Target #1: 5'-CAACCCUGACUACCAGCAG-3' (SEQ ID NO: 3023)
 EGFR-3774 19 nt Target #2: 5'-ACAACCCUGACUACCAGCA-3' (SEQ ID NO: 3283)
 EGFR-3774 19 nt Target #3: 5'-GACAACCCUGACUACCAGC-3' (SEQ ID NO: 3543)
 EGFR-3775 19 nt Target #1: 5'-AACCCUGACUACCAGCAGG-3' (SEQ ID NO: 3024)
 EGFR-3775 19 nt Target #2: 5'-CAACCCUGACUACCAGCAG-3' (SEQ ID NO: 3284)
 EGFR-3775 19 nt Target #3: 5'-ACAACCCUGACUACCAGCA-3' (SEQ ID NO: 3544)
 EGFR-3776 19 nt Target #1: 5'-ACCCUGACUACCAGCAGGA-3' (SEQ ID NO: 3025)
 EGFR-3776 19 nt Target #2: 5'-AACCCUGACUACCAGCAGG-3' (SEQ ID NO: 3285)
 EGFR-3776 19 nt Target #3: 5'-CAACCCUGACUACCAGCAG-3' (SEQ ID NO: 3545)
 EGFR-3777 19 nt Target #1: 5'-CCCUGACUACCAGCAGGAC-3' (SEQ ID NO: 3026)
 EGFR-3777 19 nt Target #2: 5'-ACCCUGACUACCAGCAGGA-3' (SEQ ID NO: 3286)
 EGFR-3777 19 nt Target #3: 5'-AACCCUGACUACCAGCAGG-3' (SEQ ID NO: 3546)
 EGFR-3778 19 nt Target #1: 5'-CCUGACUACCAGCAGGACU-3' (SEQ ID NO: 3027)
 EGFR-3778 19 nt Target #2: 5'-CCCUGACUACCAGCAGGAC-3' (SEQ ID NO: 3287)
 EGFR-3778 19 nt Target #3: 5'-ACCCUGACUACCAGCAGGA-3' (SEQ ID NO: 3547)
 EGFR-3779 19 nt Target #1: 5'-CUGACUACCAGCAGGACUU-3' (SEQ ID NO: 3028)
 EGFR-3779 19 nt Target #2: 5'-CCUGACUACCAGCAGGACU-3' (SEQ ID NO: 3288)
 EGFR-3779 19 nt Target #3: 5'-CCCUGACUACCAGCAGGAC-3' (SEQ ID NO: 3548)

Table 7: Selected Human Anti-EGFR “Blunt/Fray” DsiRNAs

5'-GGCGCAGCGCGGCCGCGCAGCAGCCUC^A-3' (SEQ ID NO: 1781)
 3'-CCGCGUCGCGCCGGCGUCGUCGGAG_G-5' (SEQ ID NO: 357)

EGFR-31 Target: 5'-GGCGCAGCGCGGCCGAGCAGCCTCCG-3' (SEQ ID NO: 713)

5'-GCGCAGCGCGGCCGAGCAGCCUCC^A-3' (SEQ ID NO: 1782)
 3'-CGCGUCGCGCCGGCGUCGUCGGAGG_C-5' (SEQ ID NO: 358)

EGFR-32 Target: 5'-GCGCAGCGCGGCCGAGCAGCCTCCG-3' (SEQ ID NO: 714)

5'-GCAGCGCGGCCGAGCAGCCUCCG^A-3' (SEQ ID NO: 1783)
 3'-CGUCGCGCCGGCGUCGUCGGAGGCG_G-5' (SEQ ID NO: 359)

EGFR-34 Target: 5'-GCAGCGCGGCCGAGCAGCCTCCGCCC-3' (SEQ ID NO: 715)

5'-CAGCGCUCCUGGCGCUGCUGGCUGC^A-3' (SEQ ID NO: 1784)
 3'-GUCGCGAGGACCGCGACGACCGACG_C-5' (SEQ ID NO: 360)

EGFR-298 Target: 5'-CAGCGCTCCTGGCGCTGCTGGCTGCGC-3' (SEQ ID NO: 716)

5'-GCGCUCCUGGCGCUGCUGGCUGCGC^C-3' (SEQ ID NO: 1785)
 3'-CGCGAGGACCGCGACGACCGACGCG_A-5' (SEQ ID NO: 361)

EGFR-300 Target: 5'-GCGCTCCTGGCGCTGCTGGCTGCGCTC-3' (SEQ ID NO: 717)

5'-GCUCCUGGCGCUGCUGGCUGCGCUC^C-3' (SEQ ID NO: 1786)
 3'-CGAGGACCGCGACGACCGACGCGAG_A-5' (SEQ ID NO: 362)

EGFR-302 Target: 5'-GCTCCTGGCGCTGCTGGCTGCGCTCTG-3' (SEQ ID NO: 718)

5'-CAGUUGGGCACUUUUGAAGAUCAUU^C-3' (SEQ ID NO: 1787)
 3'-GUCAACCCGUGAAAACUUCUAGUAA_A-5' (SEQ ID NO: 363)

EGFR-390 Target: 5'-CAGTTGGGCACCTTTTGAAGATCATTTT-3' (SEQ ID NO: 719)

5'-UGGGAAUUUGGAAAUUACCUAUGUG^A-3' (SEQ ID NO: 1788)
 3'-ACCCUUAACCUUUAUUGGAUACAC_G-5' (SEQ ID NO: 364)

EGFR-458 Target: 5'-TGGGAATTTGAAATTACCTATGTGCA-3' (SEQ ID NO: 720)

5'-AAUUAUGAUCUUUCCUUCUAAAAG^A-3' (SEQ ID NO: 1789)
 3'-UUAUACUAGAAAGGAAGAAUUUCU_G-5' (SEQ ID NO: 365)

EGFR-489 Target: 5'-AATTATGATCTTTCCTTCTTAAAGACC-3' (SEQ ID NO: 721)

5'-GUGGCUGGUUAUGUCCUCAUUGCCC^C-3' (SEQ ID NO: 1790)
 3'-CACCGACCAUACAGGAGUAACGGG_A-5' (SEQ ID NO: 366)

EGFR-525 Target: 5'-GTGGCTGGTTATGTCTCATTGCCCTC-3' (SEQ ID NO: 722)

5'-UGCCCAUGAGAAAUUUACAGGAAAU^A-3' (SEQ ID NO: 1791)

3'-ACGGGUACUCUUUAAAUGUCCUUUA_G-5', (SEQ ID NO: 367)

EGFR-676 Target: 5'-TGCCCATGAGAAATTTACAGGAAATCC-3' (SEQ ID NO: 723)

5'-CCUGCAUGGCGCCGUGCGGUUCAGC^C-3' (SEQ ID NO: 1792)

3'-GGACGUACCGCGGCACGCCAAGUCG_U-5', (SEQ ID NO: 368)

EGFR-701 Target: 5'-CCTGCATGGCGCCGTGCGGTTTCAGCAA-3' (SEQ ID NO: 724)

5'-UGGCGCCGUGCGGUUCAGCAACAAC^A-3' (SEQ ID NO: 1793)

3'-ACCGCGGCACGCCAAGUCGUUGUUG_G-5', (SEQ ID NO: 369)

EGFR-707 Target: 5'-TGGCGCCGTGCGGTTTCAGCAACAACCC-3' (SEQ ID NO: 725)

5'-UGGCGCCGUGCGGUUCAGCAACAAC^A-3' (SEQ ID NO: 1794)

3'-ACCGCGGCACGCCAAGUCGUUGUUG_G-5', (SEQ ID NO: 370)

EGFR-707 Target: 5'-TGGCGCCGTGCGGTTTCAGCAACAACCC-3' (SEQ ID NO: 726)

5'-GCGCCGUGCGGUUCAGCAACAACCC^C-3' (SEQ ID NO: 1795)

3'-CGCGGCACGCCAAGUCGUUGUUGG_A-5', (SEQ ID NO: 371)

EGFR-709 Target: 5'-GCGCCGTGCGGTTTCAGCAACAACCCTG-3' (SEQ ID NO: 727)

5'-CGCCGUGCGGUUCAGCAACAACCCU^A-3' (SEQ ID NO: 1796)

3'-GCGGCACGCCAAGUCGUUGUUGG_A-5', (SEQ ID NO: 372)

EGFR-710 Target: 5'-CGCCGTGCGGTTTCAGCAACAACCCTGC-3' (SEQ ID NO: 728)

5'-CAGCUGCCAAAAGUGUGAUCCAAGC^C-3' (SEQ ID NO: 1797)

3'-GUACGCGUUUUCACACUAGGUUCG_A-5', (SEQ ID NO: 373)

EGFR-827 Target: 5'-CAGCTGCCAAAAGTGTGATCCAAGCTG-3' (SEQ ID NO: 729)

5'-AUCUGUGCCCAGCAGUGCUCCGGGC^A-3' (SEQ ID NO: 1798)

3'-UAGACACGGGUCGUCACGAGGCCCG_C-5', (SEQ ID NO: 374)

EGFR-912 Target: 5'-ATCTGTGCCCAGCAGTGCTCCGGGCGC-3' (SEQ ID NO: 730)

5'-CUGUGCCCAGCAGUGCUCCGGGCGC^C-3' (SEQ ID NO: 1799)

3'-GACACGGGUCGUCACGAGGCCCG_A-5', (SEQ ID NO: 375)

EGFR-914 Target: 5'-CTGTGCCCAGCAGTGCTCCGGGCGCTG-3' (SEQ ID NO: 731)

5'-GUGCUCCGGGCGCUGCCGUGGCAAG^C-3' (SEQ ID NO: 1800)

3'-CACGAGGCCCGCGACGGCACCGUUC_A-5', (SEQ ID NO: 376)

EGFR-926 Target: 5'-GTGCTCCGGGCGCTGCCGTGGCAAGTC-3' (SEQ ID NO: 732)

5'-GAGAGCGACUGCCUGGUCUGCCGCA^C-3' (SEQ ID NO: 1801)
3'-CUCUCGCUGACGGACCAGACGGCGU^U-5' (SEQ ID NO: 377)

EGFR-1005 Target: 5'-GAGAGCGACTGCCTGGTCTGCCGCAA-3' (SEQ ID NO: 733)

5'-CUGCCUGGUCUGCCGCAAAUCCGA^A-3' (SEQ ID NO: 1802)
3'-GACGGACCAGACGGCGUUUAAGGCU^C-5' (SEQ ID NO: 378)

EGFR-1013 Target: 5'-CTGCCTGGTCTGCCGCAAATTCGAGA-3' (SEQ ID NO: 734)

5'-GACAGAUACGGCUCGUGCGUCCGA^A-3' (SEQ ID NO: 1803)
3'-CUGUCUAGUGCCGAGCACGCAGGCU^G-5' (SEQ ID NO: 379)

EGFR-1175 Target: 5'-GACAGATCACGGCTCGTGCGTCCGAGC-3' (SEQ ID NO: 735)

5'-CCGCAAAGUGUGUAACGGAAUAGGU^C-3' (SEQ ID NO: 1804)
3'-GGCGUUUCACACAUUGCCUUAUCCA^U-5' (SEQ ID NO: 380)

EGFR-1271 Target: 5'-CCGCAAAGTGTGTAACGGAATAGGTAT-3' (SEQ ID NO: 736)

5'-CGGAAUAGGUUAUUGGUGAAUUUAAA^A-3' (SEQ ID NO: 1805)
3'-GCCUUAUCCAUAACCACUAAAAUUU^C-5' (SEQ ID NO: 381)

EGFR-1286 Target: 5'-CGGAATAGGTATTGGTGAATTTAAAGA-3' (SEQ ID NO: 737)

5'-CUACGAAUAUUAAACACUUCAAAAA^A-3' (SEQ ID NO: 1806)
3'-GAUGC UUAUAAUUUGUGAAGUUUUU^G-5' (SEQ ID NO: 382)

EGFR-1330 Target: 5'-CTACGAATATTAAACACTTCAAAACT-3' (SEQ ID NO: 738)

5'-CCACAGGAACUGGAUAUUCUGAAAA^A-3' (SEQ ID NO: 1807)
3'-GGUGUCCUUGACCUAUAAGACUUUU^G-5' (SEQ ID NO: 383)

EGFR-1437 Target: 5'-CCACAGGAACCTGGATATTCTGAAAACC-3' (SEQ ID NO: 739)

5'-CACAGGGUUUUUGCUGAUUCAGGCU^A-3' (SEQ ID NO: 1808)
3'-GUGUCCCAAAAACGACUAAGUCCGA^A-5' (SEQ ID NO: 384)

EGFR-1475 Target: 5'-CACAGGGTTTTTGCTGATTCAGGCTTG-3' (SEQ ID NO: 740)

5'-UUCAGGAAACAAAAAUUUGUGCUAU^A-3' (SEQ ID NO: 1809)
3'-AAGUCCUUUGUUUUUAAACACGAUA^G-5' (SEQ ID NO: 385)

EGFR-1661 Target: 5'-TTCAGGAAACAAAAATTTGTGCTATGC-3' (SEQ ID NO: 741)

5'-GUGCUAUGCAAUACAAUAAACUGG^C-3' (SEQ ID NO: 1810)
3'-CACGAUACGUUUUAUGUUUUUUGACC^U-5' (SEQ ID NO: 386)

EGFR-1679 Target: 5'-GTGCTATGCAAATACAATAAACTGGAA-3' (SEQ ID NO: 742)

5'-CCGGUCAGAAAACCAAAAUUAUAAG^A-3' (SEQ ID NO: 1811)
 3'-GGCCAGUCUUUUGGUUUUAAUAUUC^G-5' (SEQ ID NO: 387)

EGFR-1723 Target: 5'-CCGGTCAGAAAACCAAAATTATAAGCA-3' (SEQ ID NO: 743)

5'-CUGCGUCUCUUGCCGGAAUGUCAGC^A-3' (SEQ ID NO: 1812)
 3'-GACGCAGAGAACGGCCUUACAGUCG^G-5' (SEQ ID NO: 388)

EGFR-1838 Target: 5'-CTGCGTCTCTTGCCGGAATGTCAGCCG-3' (SEQ ID NO: 744)

5'-GGGCCCUCUUCUUGCUGCUGGUGGU^A-3' (SEQ ID NO: 1813)
 3'-CCCGGGAGGAGAACGACGACCACCA^C-5' (SEQ ID NO: 389)

EGFR-2227 Target: 5'-GGGCCCTCCTCTTGCTGCTGGTGGTGG-3' (SEQ ID NO: 745)

5'-GGCCCUCUUCUUGCUGCUGGUGGUG^A-3' (SEQ ID NO: 1814)
 3'-CCGGGAGGAGAACGACGACCACCAC^C-5' (SEQ ID NO: 390)

EGFR-2228 Target: 5'-GGCCCTCCTCTTGCTGCTGGTGGTGGC-3' (SEQ ID NO: 746)

5'-CUCCUCUUGCUGCUGGUGGUGGCC^C-3' (SEQ ID NO: 1815)
 3'-GAGGAGAACGACGACCACCACCGGG^A-5' (SEQ ID NO: 391)

EGFR-2232 Target: 5'-CTCCTCTTGCTGCTGGTGGTGGCCCTG-3' (SEQ ID NO: 747)

5'-UCCUCUUGCUGCUGGUGGUGGCCCU^A-3' (SEQ ID NO: 1816)
 3'-AGGAGAACGACGACCACCACCGGGA^C-5' (SEQ ID NO: 392)

EGFR-2233 Target: 5'-TCCTCTTGCTGCTGGTGGTGGCCCTGG-3' (SEQ ID NO: 748)

5'-CGGAAGCGCACGCUGCGGAGGCUGC^C-3' (SEQ ID NO: 1817)
 3'-GCCUUCGCGUGCGACGCCUCCGACG^A-5' (SEQ ID NO: 393)

EGFR-2295 Target: 5'-CGGAAGCGCACGCTGCGGAGGCTGCTG-3' (SEQ ID NO: 749)

5'-AAGCGCACGCUGCGGAGGCUGCUGC^C-3' (SEQ ID NO: 1818)
 3'-UUCGCGUGCGACGCCUCCGACGACG^U-5' (SEQ ID NO: 394)

EGFR-2298 Target: 5'-AAGCGCACGCTGCGGAGGCTGCTGCAG-3' (SEQ ID NO: 750)

5'-AACUGAAUUCAAAAAGAUCAAAGUG^A-3' (SEQ ID NO: 1819)
 3'-UUGACUUAAGUUUUUCUAGUUUCAC^G-5' (SEQ ID NO: 395)

EGFR-2399 Target: 5'-AACTGAATTCAAAAAGATCAAAGTGCT-3' (SEQ ID NO: 751)

5'-CAAAGUGCUGGGCUCCGGUGCGUUC^A-3' (SEQ ID NO: 1820)
 3'-GUUUCACGACCCGAGGCCACGCAAG^C-5' (SEQ ID NO: 396)

EGFR-2417 Target: 5'-CAAAGTGCTGGGCTCCGGTTCGTTTCGG-3' (SEQ ID NO: 752)

5'-AAGUGCUGGGCUCCGGUGCGUUCGG^AC-3' (SEQ ID NO: 1821)
3'-UUCACGACCCGAGGCCACGCAAGCC^GU-5' (SEQ ID NO: 397)

EGFR-2419 Target: 5'-AAGTGCTGGGCTCCGGTTCGTTTCGGCA-3' (SEQ ID NO: 753)

5'-AGUGCUGGGCUCCGGUGCGUUCGGC^AC-3' (SEQ ID NO: 1822)
3'-UCACGACCCGAGGCCACGCAAGCC^GU-5' (SEQ ID NO: 398)

EGFR-2420 Target: 5'-AGTGCTGGGCTCCGGTTCGTTTCGGCAC-3' (SEQ ID NO: 754)

5'-GUGCUGGGCUCCGGUGCGUUCGGCA^AA-3' (SEQ ID NO: 1823)
3'-CACGACCCGAGGCCACGCAAGCC^GU-5' (SEQ ID NO: 399)

EGFR-2421 Target: 5'-GTGCTGGGCTCCGGTTCGTTTCGGCACG-3' (SEQ ID NO: 755)

5'-UGCUGGGCUCCGGUGCGUUCGGCAC^AA-3' (SEQ ID NO: 1824)
3'-ACGACCCGAGGCCACGCAAGCC^GU-5' (SEQ ID NO: 400)

EGFR-2422 Target: 5'-TGCTGGGCTCCGGTTCGTTTCGGCACGG-3' (SEQ ID NO: 756)

5'-CGUGUGCCGCCUGCUGGGCAUCUGC^AC-3' (SEQ ID NO: 1825)
3'-GCACACGGCGGACGACCCGUAGAC^GA-5' (SEQ ID NO: 401)

EGFR-2591 Target: 5'-CGTGTGCCGCTGCTGGGCATCTGCCT-3' (SEQ ID NO: 757)

5'-GUGUGCCGCCUGCUGGGCAUCUGCC^AC-3' (SEQ ID NO: 1826)
3'-CACACGGCGGACGACCCGUAGAC^GA-5' (SEQ ID NO: 402)

EGFR-2592 Target: 5'-GTGTGCCGCTGCTGGGCATCTGCCTC-3' (SEQ ID NO: 758)

5'-GUGCCGCCUGCUGGGCAUCUGCCUC^AC-3' (SEQ ID NO: 1827)
3'-CACGGCGGACGACCCGUAGAC^GAG-5' (SEQ ID NO: 403)

EGFR-2594 Target: 5'-GTGCCGCTGCTGGGCATCTGCCTCAC-3' (SEQ ID NO: 759)

5'-CACCGUGCAGCUCAUCACGCAGCUC^CC-3' (SEQ ID NO: 1828)
3'-GUGGCACGUCGAGUAGUGCGUCGAG^AU-5' (SEQ ID NO: 404)

EGFR-2624 Target: 5'-CACCGTGAGCTCATCACGCAGCTCAT-3' (SEQ ID NO: 760)

5'-CGUGCAGCUCAUCACGCAGCUCAUG^AA-3' (SEQ ID NO: 1829)
3'-GCACGUCGAGUAGUGCGUCGAGUAC^GG-5' (SEQ ID NO: 405)

EGFR-2627 Target: 5'-CGTGCAGCTCATCACGCAGCTCATGCC-3' (SEQ ID NO: 761)

5'-CAGCUCAUCACGCAGCUCAUGCCCU^AC-3' (SEQ ID NO: 1830)

3'-GUUCGAGUAGUGCGUCGAGUACGGGA_AG-5', (SEQ ID NO: 406)

EGFR-2631 Target: 5'-CAGCTCATCACGCAGCTCATGCCCTTC-3' (SEQ ID NO: 762)

5'-AGCUCAUCACGCAGCUAUGCCCUU^A-3' (SEQ ID NO: 1831)

3'-UCGAGUAGUGCGUCGAGUACGGGA_GC-5', (SEQ ID NO: 407)

EGFR-2632 Target: 5'-AGCTCATCACGCAGCTCATGCCCTTCG-3' (SEQ ID NO: 763)

5'-CAGCUAUGCCCUUCGGCUGCCUCC^CA-3' (SEQ ID NO: 1832)

3'-GUUCGAGUACGGGAAGCCGACGGAGG_AC-5', (SEQ ID NO: 408)

EGFR-2643 Target: 5'-CAGCTCATGCCCTTCGGCTGCCTCCTG-3' (SEQ ID NO: 764)

5'-AGCUAUGCCCUUCGGCUGCCUCCU^A-3' (SEQ ID NO: 1833)

3'-UCGAGUACGGGAAGCCGACGGAGG_AC-5', (SEQ ID NO: 409)

EGFR-2644 Target: 5'-AGCTCATGCCCTTCGGCTGCCTCCTGG-3' (SEQ ID NO: 765)

5'-UUGGAGGACCGUCGCUUGGUGCACC^A-3' (SEQ ID NO: 1834)

3'-AACCUCUGGCAGCGAACCACGUGG_GC-5', (SEQ ID NO: 410)

EGFR-2754 Target: 5'-TTGGAGGACCGTCGCTTGGTGCACCGC-3' (SEQ ID NO: 766)

5'-GGAGGACCGUCGCUUGGUGCACCGC^AC-3' (SEQ ID NO: 1835)

3'-CCUCCUGGCAGCGAACCACGUGGCG_U-5', (SEQ ID NO: 411)

EGFR-2756 Target: 5'-GGAGGACCGTCGCTTGGTGCACCGCGA-3' (SEQ ID NO: 767)

5'-GAGGACCGUCGCUUGGUGCACCGCG^CA-3' (SEQ ID NO: 1836)

3'-CUCCUGGCAGCGAACCACGUGGCGC_UG-5', (SEQ ID NO: 412)

EGFR-2757 Target: 5'-GAGGACCGTCGCTTGGTGCACCGCGAC-3' (SEQ ID NO: 768)

5'-AGGACCGUCGCUUGGUGCACCGCGA^A-3' (SEQ ID NO: 1837)

3'-UCCUGGCAGCGAACCACGUGGCGCU_G-5', (SEQ ID NO: 413)

EGFR-2758 Target: 5'-AGGACCGTCGCTTGGTGCACCGCGACC-3' (SEQ ID NO: 769)

5'-GACCGUCGCUUGGUGCACCGCGACC^CA-3' (SEQ ID NO: 1838)

3'-CUGGCAGCGAACCACGUGGCGCUGG_AC-5', (SEQ ID NO: 414)

EGFR-2760 Target: 5'-GACCGTCGCTTGGTGCACCGCGACCTG-3' (SEQ ID NO: 770)

5'-CCGUCGCUUGGUGCACCGCGACCUG^A-3' (SEQ ID NO: 1839)

3'-GGCAGCGAACCACGUGGCGCUGGAC_G-5', (SEQ ID NO: 415)

EGFR-2762 Target: 5'-CCGTCGCTTGGTGCACCGCGACCTGGC-3' (SEQ ID NO: 771)

5'-GUCGCUUGGUGCACC GCGACCUGGC^A-3' (SEQ ID NO: 1840)
 3'-CAGCGAACCACGUGGCGCUGGACCG^U_{C-5}' (SEQ ID NO: 416)

EGFR-2764 Target: 5'-GTCGCTTGGTGCACCGCGACCTGGCAG-3' (SEQ ID NO: 772)

5'-UCGCUUGGUGCACC GCGACCUGGCA^A-3' (SEQ ID NO: 1841)
 3'-AGCGAACCACGUGGCGCUGGACCG^U_{G-5}' (SEQ ID NO: 417)

EGFR-2765 Target: 5'-TCGCTTGGTGCACCGCGACCTGGCAGC-3' (SEQ ID NO: 773)

5'-GCUUGGUGCACC GCGACCUGGCAGC^A-3' (SEQ ID NO: 1842)
 3'-CGAACCACGUGGCGCUGGACCG^U_{G-5}' (SEQ ID NO: 418)

EGFR-2767 Target: 5'-GCTTGGTGCACCGCGACCTGGCAGCCA-3' (SEQ ID NO: 774)

5'-GGCAUUGGAAUCAAUUUUACACAGA^C-3' (SEQ ID NO: 1843)
 3'-CCGUAACCUUAGUUAAAAUGUGUCU^U_{A-5}' (SEQ ID NO: 419)

EGFR-2915 Target: 5'-GGCATTGGAATCAATTTTACACAGAAT-3' (SEQ ID NO: 775)

5'-UCAAGUGCUGGAUGAUAGACGCAGA^C-3' (SEQ ID NO: 1844)
 3'-AGUUCACGACCUACUAUCUGCGUCU^U_{A-5}' (SEQ ID NO: 420)

EGFR-3115 Target: 5'-TCAAGTGCTGGATGATAGACGCAGATA-3' (SEQ ID NO: 776)

5'-AAGUGCUGGAUGAUAGACGCAGAU^A-3' (SEQ ID NO: 1845)
 3'-UUCACGACCUACUAUCUGCGUCUAU^C_{A-5}' (SEQ ID NO: 421)

EGFR-3117 Target: 5'-AAGTGCTGGATGATAGACGCAGATAGT-3' (SEQ ID NO: 777)

5'-AGUGCUGGAUGAUAGACGCAGAUAG^C-3' (SEQ ID NO: 1846)
 3'-UCACGACCUACUAUCUGCGUCUAU^C_{A-5}' (SEQ ID NO: 422)

EGFR-3118 Target: 5'-AGTGCTGGATGATAGACGCAGATAGTC-3' (SEQ ID NO: 778)

5'-UGCUGGAUGAUAGACGCAGAUAGUC^A-3' (SEQ ID NO: 1847)
 3'-ACGACCUACUAUCUGCGUCUAUCAG^C_{G-5}' (SEQ ID NO: 423)

EGFR-3120 Target: 5'-TGCTGGATGATAGACGCAGATAGTCGC-3' (SEQ ID NO: 779)

5'-CUCCUGAGCUCUCUGAGUGCAACCA^A-3' (SEQ ID NO: 1848)
 3'-GAGGACUCGAGAGACUCACGUUGGU^C_{G-5}' (SEQ ID NO: 424)

EGFR-3372 Target: 5'-CTCCTGAGCTCTCTGAGTGCAACCAGC-3' (SEQ ID NO: 780)

5'-CUGAGCUCUCUGAGUGCAACCAGCA^C-3' (SEQ ID NO: 1849)
 3'-GACUCGAGAGACUCACGUUGGUCGU^U_{G-5}' (SEQ ID NO: 425)

EGFR-3375 Target: 5'-CTGAGCTCTCTGAGTGCAACCAGCAAC-3' (SEQ ID NO: 781)

5'-AAGCUGUCCCAUCAAGGAAGACAGC^C-3' (SEQ ID NO: 1850)
 3'-UUCGACAGGGUAGUUCUUCUGUCG^A-5' (SEQ ID NO: 426)

EGFR-3440 Target: 5'-AAGCTGTCCCATCAAGGAAGACAGCTT-3' (SEQ ID NO: 782)

5'-AGCUGUCCCAUCAAGGAAGACAGCU^A-3' (SEQ ID NO: 1851)
 3'-UCGACAGGGUAGUUCUUCUGUCG^A-5' (SEQ ID NO: 427)

EGFR-3441 Target: 5'-AGCTGTCCCATCAAGGAAGACAGCTTC-3' (SEQ ID NO: 783)

5'-AAGACAGCUUCUUGCAGCGAUACAG^A-3' (SEQ ID NO: 1852)
 3'-UUCUGUCGAAGAACGUCGCUAUGUC^G-5' (SEQ ID NO: 428)

EGFR-3457 Target: 5'-AAGACAGCTTCTTGCAGCGATACAGCT-3' (SEQ ID NO: 784)

5'-AGACAGCUUCUUGCAGCGAUACAGC^A-3' (SEQ ID NO: 1853)
 3'-UCUGUCGAAGAACGUCGCUAUGUCG^A-5' (SEQ ID NO: 429)

EGFR-3458 Target: 5'-AGACAGCTTCTTGCAGCGATACAGCTC-3' (SEQ ID NO: 785)

5'-GACAGCUUCUUGCAGCGAUACAGCU^A-3' (SEQ ID NO: 1854)
 3'-CUGUCGAAGAACGUCGCUAUGUCG^A-5' (SEQ ID NO: 430)

EGFR-3459 Target: 5'-GACAGCTTCTTGCAGCGATACAGCTCA-3' (SEQ ID NO: 786)

5'-ACAGCUUCUUGCAGCGAUACAGCUC^A-3' (SEQ ID NO: 1855)
 3'-UGUCGAAGAACGUCGCUAUGUCGAG^U-5' (SEQ ID NO: 431)

EGFR-3460 Target: 5'-ACAGCTTCTTGCAGCGATACAGCTCAG-3' (SEQ ID NO: 787)

5'-CAGCUUCUUGCAGCGAUACAGCUCA^A-3' (SEQ ID NO: 1856)
 3'-GUCGAAGAACGUCGCUAUGUCGAG^U-5' (SEQ ID NO: 432)

EGFR-3461 Target: 5'-CAGCTTCTTGCAGCGATACAGCTCAGA-3' (SEQ ID NO: 788)

5'-GCUUCUUGCAGCGAUACAGCUCAGA^A-3' (SEQ ID NO: 1857)
 3'-CGAAGAACGUCGCUAUGUCGAGUC^G-5' (SEQ ID NO: 433)

EGFR-3463 Target: 5'-GCTTCTTGCAGCGATACAGCTCAGACC-3' (SEQ ID NO: 789)

5'-CCACAAAGCAGUGAAUUUAUUGGAG^A-3' (SEQ ID NO: 1858)
 3'-GGUGUUUCGUCACUUAAAUAACCUC^G-5' (SEQ ID NO: 434)

EGFR-3876 Target: 5'-CCACAAAGCAGTGAATTTATTGGAGCA-3' (SEQ ID NO: 790)

5'-GUAUAUUUGAAAAAAAAAAAAAGUA^C-3' (SEQ ID NO: 1859)
 3'-CAUAUAAACUUUUUUUUUUUUUCAU^A-5' (SEQ ID NO: 435)

EGFR-4178 Target: 5'-GTATATTTGAAAAAAAAAAAAAGTATA-3' (SEQ ID NO: 791)

5'-UGUGAGGAUUUUUUAUUGAUUGGGGAC^A-3' (SEQ ID NO: 1860)
3'-ACACUCCUAAAAUAACUAACCCCUA_G-5' (SEQ ID NO: 436)

EGFR-4205 Target: 5'-TGTGAGGATTTTTATTGATTGGGGATC-3' (SEQ ID NO: 792)

5'-CGCUAUUGAUUUUUACUUCAAUGGGAC^C-3' (SEQ ID NO: 1861)
3'-GCGAUAAACUAAAAUGAAGUUACCCGA_A-5' (SEQ ID NO: 437)

EGFR-4249 Target: 5'-CGCTATTGATTTTTACTTCAATGGGCT-3' (SEQ ID NO: 793)

5'-AAGGAAGAAGCUUGCUGGUAGCACUC^A-3' (SEQ ID NO: 1862)
3'-UCCUUCUUCGAACGACCAUCGUGAA_A-5' (SEQ ID NO: 438)

EGFR-4284 Target: 5'-AAGGAAGAAGCTTGCTGGTAGCACTTG-3' (SEQ ID NO: 794)

5'-AGGAAGAAGCUUGCUGGUAGCACUU^A-3' (SEQ ID NO: 1863)
3'-UCCUUCUUCGAACGACCAUCGUGAA_C-5' (SEQ ID NO: 439)

EGFR-4285 Target: 5'-AGGAAGAAGCTTGCTGGTAGCACTTGC-3' (SEQ ID NO: 795)

5'-GGAAGAAGCUUGCUGGUAGCACUUG^C-3' (SEQ ID NO: 1864)
3'-CCUUCUUCGAACGACCAUCGUGAAC_G-5' (SEQ ID NO: 440)

EGFR-4286 Target: 5'-GGAAGAAGCTTGCTGGTAGCACTTGCT-3' (SEQ ID NO: 796)

5'-GAAGAAGCUUGCUGGUAGCACUUGC^C-3' (SEQ ID NO: 1865)
3'-CUUCUUCGAACGACCAUCGUGAACG_A-5' (SEQ ID NO: 441)

EGFR-4287 Target: 5'-GAAGAAGCTTGCTGGTAGCACTTGCTA-3' (SEQ ID NO: 797)

5'-AAGAAGCUUGCUGGUAGCACUUGC^A-3' (SEQ ID NO: 1866)
3'-UUCUUCGAACGACCAUCGUGAACGA_U-5' (SEQ ID NO: 442)

EGFR-4288 Target: 5'-AAGAAGCTTGCTGGTAGCACTTGCTAC-3' (SEQ ID NO: 798)

5'-GAAGCUUGCUGGUAGCACUUGC^A-3' (SEQ ID NO: 1867)
3'-CUUCGAACGACCAUCGUGAACGA_G-5' (SEQ ID NO: 443)

EGFR-4290 Target: 5'-GAAGCTTGCTGGTAGCACTTGCTACCC-3' (SEQ ID NO: 799)

5'-AAGCUUGCUGGUAGCACUUGC^A-3' (SEQ ID NO: 1868)
3'-UUCGAACGACCAUCGUGAACGA_G-5' (SEQ ID NO: 444)

EGFR-4291 Target: 5'-AAGCTTGCTGGTAGCACTTGCTACCCT-3' (SEQ ID NO: 800)

5'-AGCUUGCUGGUAGCACUUGC^A-3' (SEQ ID NO: 1869)

3'-UCGAACGACCAUCGUGAACGAUGGG_AC-5', (SEQ ID NO: 445)

EGFR-4292 Target: 5'-AGCTTGCTGGTAGCACTTGCTACCCTG-3' (SEQ ID NO: 801)

5'-GCUUGCUGGUAGCACUUGCUCACCCU_AC-3', (SEQ ID NO: 1870)

3'-CGAACGACCAUCGUGAACGAUGGG_AC_U-5', (SEQ ID NO: 446)

EGFR-4293 Target: 5'-GCTTGCTGGTAGCACTTGCTACCCTGA-3' (SEQ ID NO: 802)

5'-CUUGCUGGUAGCACUUGCUCACCCU_GC_A-3', (SEQ ID NO: 1871)

3'-GAACGACCAUCGUGAACGAUGGG_AC_UC-5', (SEQ ID NO: 447)

EGFR-4294 Target: 5'-CTTGCTGGTAGCACTTGCTACCCTGAG-3' (SEQ ID NO: 803)

5'-UUGCUGGUAGCACUUGCUCACCCU_GA_C-3', (SEQ ID NO: 1872)

3'-AACGACCAUCGUGAACGAUGGG_AC_AC-5', (SEQ ID NO: 448)

EGFR-4295 Target: 5'-TTGCTGGTAGCACTTGCTACCCTGAGT-3' (SEQ ID NO: 804)

5'-GGAUGCUUGAUUCCAGUGGUUCUGC_CC-3', (SEQ ID NO: 1873)

3'-CCUACGAACUAAGGUCACCAAGAC_GA_A-5', (SEQ ID NO: 449)

EGFR-4372 Target: 5'-GGATGCTTGATTCCAGTGGTTCTGCTT-3' (SEQ ID NO: 805)

5'-GAUGCUUGAUUCCAGUGGUUCUGC_UC_A-3', (SEQ ID NO: 1874)

3'-CUACGAACUAAGGUCACCAAGAC_GA_G-5', (SEQ ID NO: 450)

EGFR-4373 Target: 5'-GATGCTTGATTCCAGTGGTTCTGCTTC-3' (SEQ ID NO: 806)

5'-AGCAGGCCGGAUCGGUACUGUAUCA_CA-3', (SEQ ID NO: 1875)

3'-UCGUCCGGCCUAGCCAUGACAUA_GU_C-5', (SEQ ID NO: 451)

EGFR-4450 Target: 5'-AGCAGGCCGGATCGGTACTGTATCAAG-3' (SEQ ID NO: 807)

5'-GCCGGAUCGGUACUGUAUCAAGUCA_CA-3', (SEQ ID NO: 1876)

3'-CGGCCUAGCCAUGACAUA_GU_CU_AC-5', (SEQ ID NO: 452)

EGFR-4455 Target: 5'-GCCGGATCGGTACTGTATCAAGTCATG-3' (SEQ ID NO: 808)

5'-UCCUUAGACUUACUUUUGUAAAAU_AC-3', (SEQ ID NO: 1877)

3'-AGGAAUCUGAAUGAAAA_ACAUUUUU_AC_A-5', (SEQ ID NO: 453)

EGFR-4550 Target: 5'-TCCTTAGACTTACTTTTGTAATAATGT-3' (SEQ ID NO: 809)

5'-CUGUCUUGCUGUCAUGAAAUCAGCA_CA-3', (SEQ ID NO: 1878)

3'-GACAGAACGACAGUACUUUAGUC_GU_C-5', (SEQ ID NO: 454)

EGFR-4684 Target: 5'-CTGTCTTGCTGTCATGAAATCAGCAAG-3' (SEQ ID NO: 810)

5'-CCUAAGGAUAGCACCGCUUUUGUUC^A-3' (SEQ ID NO: 1879)
 3'-GGAUCCUAUCGUGGCGAAAAACAAG_A-5' (SEQ ID NO: 455)

EGFR-4804 Target: 5'-CCTAAGGATAGCACCGCTTTTGTTC-3' (SEQ ID NO: 811)

5'-UAAGGAUAGCACCGCUUUUGUUCUC^A-3' (SEQ ID NO: 1880)
 3'-AUCCUAUCGUGGCGAAAAACAAGAG_C-5' (SEQ ID NO: 456)

EGFR-4806 Target: 5'-TAAGGATAGCACCGCTTTTGTTC-3' (SEQ ID NO: 812)

5'-AAGGAUAGCACCGCUUUUGUUCUCG^A-3' (SEQ ID NO: 1881)
 3'-UCCUAUCGUGGCGAAAAACAAGAGC_G-5' (SEQ ID NO: 457)

EGFR-4807 Target: 5'-AAGGATAGCACCGCTTTTGTTC-3' (SEQ ID NO: 813)

5'-AGGAUAGCACCGCUUUUGUUCUCGC^C-3' (SEQ ID NO: 1882)
 3'-UCCUAUCGUGGCGAAAAACAAGAGCG_U-5' (SEQ ID NO: 458)

EGFR-4808 Target: 5'-AGGATAGCACCGCTTTTGTTC-3' (SEQ ID NO: 814)

5'-GGAUAGCACCGCUUUUGUUCUCGCA^C-3' (SEQ ID NO: 1883)
 3'-CCUAUCGUGGCGAAAAACAAGAGCGU_U-5' (SEQ ID NO: 459)

EGFR-4809 Target: 5'-GGATAGCACCGCTTTTGTTC-3' (SEQ ID NO: 815)

5'-GAUAGCACCGCUUUUGUUCUCGCA^C-3' (SEQ ID NO: 1884)
 3'-CUAUCGUGGCGAAAAACAAGAGCGUU_U-5' (SEQ ID NO: 460)

EGFR-4810 Target: 5'-GATAGCACCGCTTTTGTTC-3' (SEQ ID NO: 816)

5'-AUAGCACCGCUUUUGUUCUCGCA^C-3' (SEQ ID NO: 1885)
 3'-UAUCGUGGCGAAAAACAAGAGCGUUU_U-5' (SEQ ID NO: 461)

EGFR-4811 Target: 5'-ATAGCACCGCTTTTGTTC-3' (SEQ ID NO: 817)

5'-UAGCACCGCUUUUGUUCUCGCA^A-3' (SEQ ID NO: 1886)
 3'-AUCGUGGCGAAAAACAAGAGCGUUU_G-5' (SEQ ID NO: 462)

EGFR-4812 Target: 5'-TAGCACCGCTTTTGTTC-3' (SEQ ID NO: 818)

5'-AGCACCGCUUUUGUUCUCGCA^A-3' (SEQ ID NO: 1887)
 3'-UCGUGGCGAAAAACAAGAGCGUUUU_G-5' (SEQ ID NO: 463)

EGFR-4813 Target: 5'-AGCACCGCTTTTGTTC-3' (SEQ ID NO: 819)

5'-ACCGCUUUUGUUCUCGCA^A-3' (SEQ ID NO: 1888)
 3'-UGGCGAAAAACAAGAGCGUUUUUGCA_A-5' (SEQ ID NO: 464)

EGFR-4816 Target: 5'-ACCGCTTTTGTTC-3' (SEQ ID NO: 820)

5'-CCGCUUUUGUUCUCGCAAAAACGUAC^A-3' (SEQ ID NO: 1889)
 3'-GGCGAAAACAAGAGCGUUUUUGCAUA_A-5' (SEQ ID NO: 465)

EGFR-4817 Target: 5'-CCGCTTTTGTTCCTCGCAAAAACGTATC-3' (SEQ ID NO: 821)

5'-CGCUUUUGUUCUCGCAAAAACGUAU^A-3' (SEQ ID NO: 1890)
 3'-GCGAAAACAAGAGCGUUUUUGCAUA_A-5' (SEQ ID NO: 466)

EGFR-4818 Target: 5'-CGCTTTTGTTCCTCGCAAAAACGTATCT-3' (SEQ ID NO: 822)

5'-GCUUUUGUUCUCGCAAAAACGUAU^C-3' (SEQ ID NO: 1891)
 3'-CGAAAACAAGAGCGUUUUUGCAUAG_A-5' (SEQ ID NO: 467)

EGFR-4819 Target: 5'-GCTTTTGTTCCTCGCAAAAACGTATCTC-3' (SEQ ID NO: 823)

5'-UGUUCUCGCAAAAACGUAUCCUA^C-3' (SEQ ID NO: 1892)
 3'-ACAAGAGCGUUUUUGCAUAGAGGAU_A-5' (SEQ ID NO: 468)

EGFR-4824 Target: 5'-TGTTCTCGCAAAAACGTATCTCCTAAT-3' (SEQ ID NO: 824)

5'-CAAAAUUAGUUUGUGUUACUUAUGG^C-3' (SEQ ID NO: 1893)
 3'-GUUUUAAUCAAAACACAAUGAAUACC_U-5' (SEQ ID NO: 469)

EGFR-4953 Target: 5'-CAAAATTAGTTTGTGTTACTTATGGAA-3' (SEQ ID NO: 825)

5'-ACUUAUGGAAGAUAGUUUUCUCCU^C-3' (SEQ ID NO: 1894)
 3'-UGAAUACCUUCUAUCAAAGAGGAA_A-5' (SEQ ID NO: 470)

EGFR-4970 Target: 5'-ACTTATGGAAGATAGTTTTCTCCTTTT-3' (SEQ ID NO: 826)

5'-CUUCAAAAGCUUUUACUCAAGAG^C-3' (SEQ ID NO: 1895)
 3'-GAAGUUUUCGAAAAAUGAGUUUCUC_A-5' (SEQ ID NO: 471)

EGFR-5003 Target: 5'-CTTCAAAGCTTTTTACTCAAAGAGTA-3' (SEQ ID NO: 827)

5'-AAACUAGGGUUUGAAAUUGAUAAUG^A-3' (SEQ ID NO: 1896)
 3'-UUUGAUCCCAAACUUUAACUAAUAC_G-5' (SEQ ID NO: 472)

EGFR-5206 Target: 5'-AAACTAGGGTTTGAAATTGATAATGCT-3' (SEQ ID NO: 828)

5'-CCUAAAAUAAUUCUCUACAAUUGG^C-3' (SEQ ID NO: 1897)
 3'-GGAUUUUUAAUAAAGAGAUGUUAACC_U-5' (SEQ ID NO: 473)

EGFR-5275 Target: 5'-CCTAAATAATTTCTCTACAATTGGAA-3' (SEQ ID NO: 829)

5'-AACAGCAGUCCUUUGUAAACAGUGU^C-3' (SEQ ID NO: 1898)
 3'-UUGUCGUCAGGAAACAUUUGUCACA_A-5' (SEQ ID NO: 474)

EGFR-5374 Target: 5'-AACAGCAGTCCTTTGTAAACAGTGTTT-3' (SEQ ID NO: 830)

5'-UCCAAUUUAUCAAGGAAGAAAUGGU^CA-3' (SEQ ID NO: 1899)
3'-AGGUUAAAAGUUCUUCUUUACCA_AG-5' (SEQ ID NO: 475)

EGFR-5429 Target: 5'-TCCAATTTATCAAGGAAGAAATGGTTC-3' (SEQ ID NO: 831)

5'-CAUACAAAAUGUUCUUCUUUGCUUUU^CC-3' (SEQ ID NO: 1900)
3'-GUAUGUUUACAAGGAAACGAAAA_UU-5' (SEQ ID NO: 476)

EGFR-5497 Target: 5'-CATACAAAATGTTCCCTTTTGCTTTTAA-3' (SEQ ID NO: 832)

5'-AUGUCCUUUUGCUUUUAAAGUAAU^CC-3' (SEQ ID NO: 1901)
3'-UACAAGGAAACGAAAAUUUCAUUA_AA-5' (SEQ ID NO: 477)

EGFR-5505 Target: 5'-ATGTTCCCTTTTGCTTTTAAAGTAATTT-3' (SEQ ID NO: 833)

5'-UGUCCUUUUGCUUUUAAAGUAAU^CC-3' (SEQ ID NO: 1902)
3'-ACAAGGAAACGAAAAUUUCAUUA_AA-5' (SEQ ID NO: 478)

EGFR-5506 Target: 5'-TGTTCCCTTTTGCTTTTAAAGTAATTTT-3' (SEQ ID NO: 834)

5'-UUUUGCUUUUAAAGUAAUUUUUGAC^CA-3' (SEQ ID NO: 1903)
3'-AAAACGAAAAUUUCAUUA_AAAACUG_A-5' (SEQ ID NO: 479)

EGFR-5512 Target: 5'-TTTTGCTTTTAAAGTAATTTTGAATC-3' (SEQ ID NO: 835)

5'-UUGUUAAGAAAGUAAUUUGAUUUUUG^CA-3' (SEQ ID NO: 1904)
3'-AACAAUUCUUUCAUAAACUAAAAAC_AG-5' (SEQ ID NO: 480)

EGFR-5565 Target: 5'-TTGTTAAGAAAGTATTTGATTTTGTGTC-3' (SEQ ID NO: 836)

5'-AUUUGGAAAUUACCUAUGUGCAGAG^AC-3' (SEQ ID NO: 1905)
3'-UAAACCUUUAUGGAUACACGUCUC_CU-5' (SEQ ID NO: 481)

EGFR-463 Target: 5'-ATTTGGAAATTACCTATGTGCAGAGGA-3' (SEQ ID NO: 837)

5'-UUUGGAAAUUACCUAUGUGCAGAGG^CC-3' (SEQ ID NO: 1906)
3'-AAACCUUUAUGGAUACACGUCUCC_UU-5' (SEQ ID NO: 482)

EGFR-464 Target: 5'-TTTGGAAATTACCTATGTGCAGAGGAA-3' (SEQ ID NO: 838)

5'-AUCUUCCUUCUUAAGACCAUCCA^AA-3' (SEQ ID NO: 1907)
3'-UAGAAAGGAAGAAUUCUGGUAGGU_CC-5' (SEQ ID NO: 483)

EGFR-496 Target: 5'-ATCTTTCCTTCTTAAAGACCATCCAGG-3' (SEQ ID NO: 839)

5'-UCUUCCUUCUUAAGACCAUCCAG^AC-3' (SEQ ID NO: 1908)

3'-AGAAAGGAAGAAUUUCUGGUAGGUC_{U-5'}, (SEQ ID NO: 484)

EGFR-497 Target: 5'-TCTTTCCTTCTTAAAGACCATCCAGGA-3' (SEQ ID NO: 840)

5'-CUUCCUUCUUAAGACCAUCCAGG^A-3' (SEQ ID NO: 1909)

3'-GAAAGGAAGAAUUUCUGGUAGGUCC_{U-5'}, (SEQ ID NO: 485)

EGFR-498 Target: 5'-CTTTCCTTCTTAAAGACCATCCAGGAG-3' (SEQ ID NO: 841)

5'-UUUCCUUCUUAAGACCAUCCAGGA^A-3' (SEQ ID NO: 1910)

3'-AAAGGAAGAAUUUCUGGUAGGUCC_{C-5'}, (SEQ ID NO: 486)

EGFR-499 Target: 5'-TTTCCTTCTTAAAGACCATCCAGGAGG-3' (SEQ ID NO: 842)

5'-UUCUUCUUAAGACCAUCCAGGAG^A-3' (SEQ ID NO: 1911)

3'-AAGGAAGAAUUUCUGGUAGGUCC_{C-5'}, (SEQ ID NO: 487)

EGFR-500 Target: 5'-TTCCTTCTTAAAGACCATCCAGGAGGT-3' (SEQ ID NO: 843)

5'-UCCUUCUUAAGACCAUCCAGGAGG^A-3' (SEQ ID NO: 1912)

3'-AGGAAGAAUUUCUGGUAGGUCC_{A-5'}, (SEQ ID NO: 488)

EGFR-501 Target: 5'-TCCTTCTTAAAGACCATCCAGGAGGTG-3' (SEQ ID NO: 844)

5'-CCUUCUUAAGACCAUCCAGGAGGU^A-3' (SEQ ID NO: 1913)

3'-GGAAGAAUUUCUGGUAGGUCC_{C-5'}, (SEQ ID NO: 489)

EGFR-502 Target: 5'-CCTTCTTAAAGACCATCCAGGAGGTGG-3' (SEQ ID NO: 845)

5'-CUUCUUAAGACCAUCCAGGAGGUG^A-3' (SEQ ID NO: 1914)

3'-GAAGAAUUUCUGGUAGGUCC_{C-5'}, (SEQ ID NO: 490)

EGFR-503 Target: 5'-CTTCTTAAAGACCATCCAGGAGGTGGC-3' (SEQ ID NO: 846)

5'-UUCUUAAGACCAUCCAGGAGGUGG^A-3' (SEQ ID NO: 1915)

3'-AAGAAUUUCUGGUAGGUCC_{A-5'}, (SEQ ID NO: 491)

EGFR-504 Target: 5'-TTCTTAAAGACCATCCAGGAGGTGGCT-3' (SEQ ID NO: 847)

5'-UCUUAAGACCAUCCAGGAGGUGGC^A-3' (SEQ ID NO: 1916)

3'-AGAAUUUCUGGUAGGUCC_{A-5'}, (SEQ ID NO: 492)

EGFR-505 Target: 5'-TCTTAAAGACCATCCAGGAGGTGGCTG-3' (SEQ ID NO: 848)

5'-CUUAAGACCAUCCAGGAGGUGGCU^A-3' (SEQ ID NO: 1917)

3'-GAAUUUCUGGUAGGUCC_{C-5'}, (SEQ ID NO: 493)

EGFR-506 Target: 5'-CTTAAAGACCATCCAGGAGGTGGCTGG-3' (SEQ ID NO: 849)

5'-UAAAAGACCAUCCAGGAGGUGGCUG^AC-3' (SEQ ID NO: 1918)
3'-AAUUCUGGUAGGUCCUCCACCGAC_A-5' (SEQ ID NO: 494)

EGFR-507 Target: 5'-TTAAAGACCATCCAGGAGGTGGCTGGT-3' (SEQ ID NO: 850)

5'-UAAAGACCAUCCAGGAGGUGGCUGG^CC-3' (SEQ ID NO: 1919)
3'-AUUUCUGGUAGGUCCUCCACCGACC_A-5' (SEQ ID NO: 495)

EGFR-508 Target: 5'-TAAAGACCATCCAGGAGGTGGCTGGTT-3' (SEQ ID NO: 851)

5'-AAAGACCAUCCAGGAGGUGGCUGGU^CC-3' (SEQ ID NO: 1920)
3'-UUUCUGGUAGGUCCUCCACCGACCA_A-5' (SEQ ID NO: 496)

EGFR-509 Target: 5'-AAAGACCATCCAGGAGGTGGCTGGTTA-3' (SEQ ID NO: 852)

5'-AGUGUGAUCCAAGCUGUCCCAAUGG^AC-3' (SEQ ID NO: 1921)
3'-UCACACUAGGUUCGACAGGGUUACC_U-5' (SEQ ID NO: 497)

EGFR-838 Target: 5'-AGTGTGATCCAAGCTGTCCCAATGGGA-3' (SEQ ID NO: 853)

5'-GUGUGAUCCAAGCUGUCCCAAUGGG^CA-3' (SEQ ID NO: 1922)
3'-CACACUAGGUUCGACAGGGUUACCC_U-5' (SEQ ID NO: 498)

EGFR-839 Target: 5'-GTGTGATCCAAGCTGTCCCAATGGGAG-3' (SEQ ID NO: 854)

5'-UGUGAUCCAAGCUGUCCCAAUGGGA^AA-3' (SEQ ID NO: 1923)
3'-ACACUAGGUUCGACAGGGUUACCCU_C-5' (SEQ ID NO: 499)

EGFR-840 Target: 5'-TGTGATCCAAGCTGTCCCAATGGGAGC-3' (SEQ ID NO: 855)

5'-GUGAUCCAAGCUGUCCCAAUGGGAG^AC-3' (SEQ ID NO: 1924)
3'-CACUAGGUUCGACAGGGUUACCCUC_G-5' (SEQ ID NO: 500)

EGFR-841 Target: 5'-GTGATCCAAGCTGTCCCAATGGGAGCT-3' (SEQ ID NO: 856)

5'-UGAUCCAAGCUGUCCCAAUGGGAGC^AA-3' (SEQ ID NO: 1925)
3'-ACUAGGUUCGACAGGGUUACCCUCG_A-5' (SEQ ID NO: 501)

EGFR-842 Target: 5'-TGATCCAAGCTGTCCCAATGGGAGCTG-3' (SEQ ID NO: 857)

5'-GCAGGAGAGGAGAACUGCCAGAAAC^CA-3' (SEQ ID NO: 1926)
3'-CGUCCUCUCCUCUUGACGGUCUUUG_A-5' (SEQ ID NO: 502)

EGFR-876 Target: 5'-GCAGGAGAGGAGAACTGCCAGAACTG-3' (SEQ ID NO: 858)

5'-CAGGAGAGGAGAACUGCCAGAAACU^AC-3' (SEQ ID NO: 1927)
3'-GUCCUCUCCUCUUGACGGUCUUUGA_C-5' (SEQ ID NO: 503)

EGFR-877 Target: 5'-CAGGAGAGGAGAACTGCCAGAACTGA-3' (SEQ ID NO: 859)

5'-AGGAGAGGAGAACUGCCAGAAACUG^CA-3' (SEQ ID NO: 1928)
 3'-UCCUCUCCUCUUGACGGUCUUUGAC^UG-5' (SEQ ID NO: 504)

EGFR-878 Target: 5'-AGGAGAGGAGAACTGCCAGAACTGAC-3' (SEQ ID NO: 860)

5'-GGAGAGGAGAACUGCCAGAAACUGA^AA-3' (SEQ ID NO: 1929)
 3'-CCUCUCCUCUUGACGGUCUUUGAC^UG-5' (SEQ ID NO: 505)

EGFR-879 Target: 5'-GGAGAGGAGAACTGCCAGAACTGACC-3' (SEQ ID NO: 861)

5'-ACUGACCAAAAUCAUCUGUGCCCAG^AC-3' (SEQ ID NO: 1930)
 3'-UGACUGGUUUUAGUAGACACGGGUC^GU-5' (SEQ ID NO: 506)

EGFR-899 Target: 5'-ACTGACCAAAATCATCTGTGCCCAGCA-3' (SEQ ID NO: 862)

5'-CUGACCAAAAUCAUCUGUGCCCAGC^AA-3' (SEQ ID NO: 1931)
 3'-GACUGGUUUUAGUAGACACGGGUCG^UC-5' (SEQ ID NO: 507)

EGFR-900 Target: 5'-CTGACCAAAATCATCTGTGCCCAGCAG-3' (SEQ ID NO: 863)

5'-UGACCAAAAUCAUCUGUGCCCAGCA^AC-3' (SEQ ID NO: 1932)
 3'-ACUGGUUUUAGUAGACACGGGUCG^UC_A-5' (SEQ ID NO: 508)

EGFR-901 Target: 5'-TGACCAAAATCATCTGTGCCCAGCAGT-3' (SEQ ID NO: 864)

5'-GACCAAAAUCAUCUGUGCCCAGCAG^AC-3' (SEQ ID NO: 1933)
 3'-CUGGUUUUAGUAGACACGGGUCG^UC_A-5' (SEQ ID NO: 509)

EGFR-902 Target: 5'-GACCAAAATCATCTGTGCCCAGCAGTG-3' (SEQ ID NO: 865)

5'-ACCAAAAUCAUCUGUGCCCAGCAGU^AA-3' (SEQ ID NO: 1934)
 3'-UGGUUUUAGUAGACACGGGUCG^UC_A-5' (SEQ ID NO: 510)

EGFR-903 Target: 5'-ACCAAAATCATCTGTGCCCAGCAGTGC-3' (SEQ ID NO: 866)

5'-CCAAAAUCAUCUGUGCCCAGCAGUG^AC-3' (SEQ ID NO: 1935)
 3'-GGUUUUAGUAGACACGGGUCG^UC_A-5' (SEQ ID NO: 511)

EGFR-904 Target: 5'-CCAAATCATCTGTGCCCAGCAGTGCT-3' (SEQ ID NO: 867)

5'-CAAAAUCAUCUGUGCCCAGCAGUGC^AC-3' (SEQ ID NO: 1936)
 3'-GUUUUAGUAGACACGGGUCG^UC_A-5' (SEQ ID NO: 512)

EGFR-905 Target: 5'-CAAAATCATCTGTGCCCAGCAGTGCTC-3' (SEQ ID NO: 868)

5'-CCCAGUGACUGCUGCCACAACCAGU^AC-3' (SEQ ID NO: 1937)
 3'-GGGUCACUGACGACGGUGUUGGUCA^AC-5' (SEQ ID NO: 513)

EGFR-954 Target: 5'-CCCAGTGACTGCTGCCACAACCAGTGT-3' (SEQ ID NO: 869)

5'-CCAGUGACUGCUGCCACAACCAGUG^CA-3' (SEQ ID NO: 1938)
 3'-GGUCACUGACGACGGUGUUGGUCAC^AC-5' (SEQ ID NO: 514)

EGFR-955 Target: 5'-CCAGTGACTGCTGCCACAACCAGTGTG-3' (SEQ ID NO: 870)

5'-CAGUGACUGCUGCCACAACCAGUGU^AA-3' (SEQ ID NO: 1939)
 3'-GUCACUGACGACGGUGUUGGUCACA^CG-5' (SEQ ID NO: 515)

EGFR-956 Target: 5'-CAGTGACTGCTGCCACAACCAGTGTGC-3' (SEQ ID NO: 871)

5'-CUCACUCUCCAUAAAUGCUACGAAU^CC-3' (SEQ ID NO: 1940)
 3'-GAGUGAGAGGUAAUUUACGAUGCUUA^UA-5' (SEQ ID NO: 516)

EGFR-1313 Target: 5'-CTCACTCTCCATAAATGCTACGAATAT-3' (SEQ ID NO: 872)

5'-GGUUUUUGCUGAUUCAGGCUUGGCC^CA-3' (SEQ ID NO: 1941)
 3'-CCAAAAACGACUAAGUCCGAACCGG^AC-5' (SEQ ID NO: 517)

EGFR-1480 Target: 5'-GGTTTTTGCTGATTCAGGCTTGGCCTG-3' (SEQ ID NO: 873)

5'-GUUUUUGCUGAUUCAGGCUUGGCCU^AC-3' (SEQ ID NO: 1942)
 3'-CAAAAACGACUAAGUCCGAACCGGA^CU-5' (SEQ ID NO: 518)

EGFR-1481 Target: 5'-GTTTTTGCTGATTCAGGCTTGGCCTGA-3' (SEQ ID NO: 874)

5'-UUUUUUGCUGAUUCAGGCUUGGCCUG^CC-3' (SEQ ID NO: 1943)
 3'-AAAAACGACUAAGUCCGAACCGGAC^UU-5' (SEQ ID NO: 519)

EGFR-1482 Target: 5'-TTTTTGCTGATTCAGGCTTGGCCTGAA-3' (SEQ ID NO: 875)

5'-UUUUGCUGAUUCAGGCUUGGCCUGA^CC-3' (SEQ ID NO: 1944)
 3'-AAAACGACUAAGUCCGAACCGGACU^UU-5' (SEQ ID NO: 520)

EGFR-1483 Target: 5'-TTTTGCTGATTCAGGCTTGGCCTGAAA-3' (SEQ ID NO: 876)

5'-UUUGCUGAUUCAGGCUUGGCCUGAA^CC-3' (SEQ ID NO: 1945)
 3'-AAACGACUAAGUCCGAACCGGACUU^UU-5' (SEQ ID NO: 521)

EGFR-1484 Target: 5'-TTTGCTGATTCAGGCTTGGCCTGAAAA-3' (SEQ ID NO: 877)

5'-UUGCUGAUUCAGGCUUGGCCUGAAA^CA-3' (SEQ ID NO: 1946)
 3'-AACGACUAAGUCCGAACCGGACUUU^UG-5' (SEQ ID NO: 522)

EGFR-1485 Target: 5'-TTGCTGATTCAGGCTTGGCCTGAAAAC-3' (SEQ ID NO: 878)

5'-UGCUGAUUCAGGCUUGGCCUGAAAA^AC-3' (SEQ ID NO: 1947)

3'-ACGACUAAGUCCGAACCGGACUUUU_GU-5', (SEQ ID NO: 523)

EGFR-1486 Target: 5'-TGCTGATTGAGGCTTGGCCTGAAAACA-3' (SEQ ID NO: 879)

5'-GCUGAUUCAGGCUUGGCCUGAAAAC^CA-3' (SEQ ID NO: 1948)

3'-CGACUAAGUCCGAACCGGACUUUU_GU_C-5', (SEQ ID NO: 524)

EGFR-1487 Target: 5'-GCTGATTGAGGCTTGGCCTGAAAACAG-3' (SEQ ID NO: 880)

5'-CCAAGCAACAUGGUCAGUUUUUCUCU^CA-3' (SEQ ID NO: 1949)

3'-GGUUCGUUGUACCAGUCAAAAGAGAA_AC-5', (SEQ ID NO: 525)

EGFR-1561 Target: 5'-CCAAGCAACATGGTCAGTTTTCTCTTG-3' (SEQ ID NO: 881)

5'-CAAGCAACAUGGUCAGUUUUUCUCUU^AA-3' (SEQ ID NO: 1950)

3'-GUUCGUUGUACCAGUCAAAAGAGAA_CG-5', (SEQ ID NO: 526)

EGFR-1562 Target: 5'-CAAGCAACATGGTCAGTTTTCTCTTGC-3' (SEQ ID NO: 882)

5'-AAGCAACAUGGUCAGUUUUUCUCUUG^AC-3' (SEQ ID NO: 1951)

3'-UUCGUUGUACCAGUCAAAAGAGAA_CG_U-5', (SEQ ID NO: 527)

EGFR-1563 Target: 5'-AAGCAACATGGTCAGTTTTCTCTTGCA-3' (SEQ ID NO: 883)

5'-UACAAUAAACUGGAAAAAACUGUUU^AA-3' (SEQ ID NO: 1952)

3'-AUGUUAUUUGACCUUUUUUGACAAA_CC-5', (SEQ ID NO: 528)

EGFR-1691 Target: 5'-TACAATAAACTGGAAAAAACTGTTTGG-3' (SEQ ID NO: 884)

5'-CUCAGGCCAUGAACAUCACCUGCAC^CA-3' (SEQ ID NO: 1953)

3'-GAGUCCGGUACUUGUAGUGGACGUG_UC-5', (SEQ ID NO: 529)

EGFR-1963 Target: 5'-CTCAGGCCATGAACATCACCTGCACAG-3' (SEQ ID NO: 885)

5'-UCAGGCCAUGAACAUCACCUGCACA^AA-3' (SEQ ID NO: 1954)

3'-AGUCCGGUACUUGUAGUGGACGUGU_CC-5', (SEQ ID NO: 530)

EGFR-1964 Target: 5'-TCAGGCCATGAACATCACCTGCACAGG-3' (SEQ ID NO: 886)

5'-GUAUCCAGUGUGCCCACUACAUUGA^AA-3' (SEQ ID NO: 1955)

3'-CAUAGGUCACACGGGUGAUGUAACU_GC-5', (SEQ ID NO: 531)

EGFR-2008 Target: 5'-GTATCCAGTGTGCCCCACTACATTGACG-3' (SEQ ID NO: 887)

5'-UAUCCAGUGUGCCCACUACAUUGAC^AA-3' (SEQ ID NO: 1956)

3'-AUAGGUCACACGGGUGAUGUAACUG_CC-5', (SEQ ID NO: 532)

EGFR-2009 Target: 5'-TATCCAGTGTGCCCCACTACATTGACGG-3' (SEQ ID NO: 888)

5'-AUCCAGUGUGCCCACUACAUUGACG^A-3' (SEQ ID NO: 1957)
 3'-UAGGUCACACGGGUGAUGUAACUGC_G-5' (SEQ ID NO: 533)

EGFR-2010 Target: 5'-ATCCAGTGTGCCCCACTACATTGACGGC-3' (SEQ ID NO: 889)

5'-UCCAGUGUGCCCACUACAUUGACGG^A-3' (SEQ ID NO: 1958)
 3'-AGGUCACACGGGUGAUGUAACUGCC_G-5' (SEQ ID NO: 534)

EGFR-2011 Target: 5'-TCCAGTGTGCCCCACTACATTGACGGCC-3' (SEQ ID NO: 890)

5'-CCAGUGUGCCCACUACAUUGACGGC^A-3' (SEQ ID NO: 1959)
 3'-GGUCACACGGGUGAUGUAACUGCCG_G-5' (SEQ ID NO: 535)

EGFR-2012 Target: 5'-CCAGTGTGCCCCACTACATTGACGGCCC-3' (SEQ ID NO: 891)

5'-CUGAAUUCAAAAAGAUCAAAGUGCU^A-3' (SEQ ID NO: 1960)
 3'-GACUUAAGUUUUUCUAGUUUCACGA_C-5' (SEQ ID NO: 536)

EGFR-2401 Target: 5'-CTGAATTCAAAAAGATCAAAGTGCTGG-3' (SEQ ID NO: 892)

5'-UGAAUUCAAAAAGAUCAAAGUGCUG^A-3' (SEQ ID NO: 1961)
 3'-ACUUAAGUUUUUCUAGUUUCACGAC_C-5' (SEQ ID NO: 537)

EGFR-2402 Target: 5'-TGAATTCAAAAAGATCAAAGTGCTGGG-3' (SEQ ID NO: 893)

5'-GACUCUGGAUCCCAGAAGGUGAGAA^C-3' (SEQ ID NO: 1962)
 3'-CUGAGACCUAGGGUCUCCACUCUU_U-5' (SEQ ID NO: 538)

EGFR-2458 Target: 5'-GACTCTGGATCCCAGAAGGTGAGAAAG-3' (SEQ ID NO: 894)

5'-ACUCUGGAUCCCAGAAGGUGAGAAA^A-3' (SEQ ID NO: 1963)
 3'-UGAGACCUAGGGUCUCCACUCUU_A-5' (SEQ ID NO: 539)

EGFR-2459 Target: 5'-ACTCTGGATCCCAGAAGGTGAGAAAGT-3' (SEQ ID NO: 895)

5'-CUCUGGAUCCCAGAAGGUGAGAAAAG^C-3' (SEQ ID NO: 1964)
 3'-GAGACCUAGGGUCUCCACUCUU_A-5' (SEQ ID NO: 540)

EGFR-2460 Target: 5'-CTCTGGATCCCAGAAGGTGAGAAAGTT-3' (SEQ ID NO: 896)

5'-UCUGGAUCCCAGAAGGUGAGAAAAGU^C-3' (SEQ ID NO: 1965)
 3'-AGACCUAGGGUCUCCACUCUU_A-5' (SEQ ID NO: 541)

EGFR-2461 Target: 5'-TCTGGATCCCAGAAGGTGAGAAAGTTA-3' (SEQ ID NO: 897)

5'-CUGGAUCCCAGAAGGUGAGAAAAGUU^C-3' (SEQ ID NO: 1966)
 3'-GACCUAGGGUCUCCACUCUU_U-5' (SEQ ID NO: 542)

EGFR-2462 Target: 5'-CTGGATCCCAGAAGGTGAGAAAGTTAA-3' (SEQ ID NO: 898)

5'-UGGAUCCCAGAAGGUGAGAAAGUUA^C-3' (SEQ ID NO: 1967)
 3'-ACCUAGGGUCUUCCACUCUUUCAAU^U-5' (SEQ ID NO: 543)

EGFR-2463 Target: 5'-TGGATCCCAGAAGGTGAGAAAGTTAAA-3' (SEQ ID NO: 899)

5'-GGAUCCCAGAAGGUGAGAAAGUUA^C-3' (SEQ ID NO: 1968)
 3'-CCUAGGGUCUUCCACUCUUUCAAU^U-5' (SEQ ID NO: 544)

EGFR-2464 Target: 5'-GGATCCCAGAAGGTGAGAAAGTTAAAA-3' (SEQ ID NO: 900)

5'-GAUCCCAGAAGGUGAGAAAGUUA^C-3' (SEQ ID NO: 1969)
 3'-CUAGGGUCUUCCACUCUUUCAAU^U-5' (SEQ ID NO: 545)

EGFR-2465 Target: 5'-GATCCCAGAAGGTGAGAAAGTTAAAAT-3' (SEQ ID NO: 901)

5'-CGCAGCAUGUCAAGAUCACAGAUUU^C-3' (SEQ ID NO: 1970)
 3'-GCGUCGUACAGUUCUAGUGUCUAAA^A-5' (SEQ ID NO: 546)

EGFR-2815 Target: 5'-CGCAGCATGTCAAGATCACAGATTTTG-3' (SEQ ID NO: 902)

5'-GCAGCAUGUCAAGAUCACAGAUUUU^A-3' (SEQ ID NO: 1971)
 3'-CGUCGUACAGUUCUAGUGUCUAAAA^C-5' (SEQ ID NO: 547)

EGFR-2816 Target: 5'-GCAGCATGTCAAGATCACAGATTTTGG-3' (SEQ ID NO: 903)

5'-CAGCAUGUCAAGAUCACAGAUUUUG^A-3' (SEQ ID NO: 1972)
 3'-GUCGUACAGUUCUAGUGUCUAAAAC^C-5' (SEQ ID NO: 548)

EGFR-2817 Target: 5'-CAGCATGTCAAGATCACAGATTTTGGG-3' (SEQ ID NO: 904)

5'-AGCAUGUCAAGAUCACAGAUUUUGG^A-3' (SEQ ID NO: 1973)
 3'-UCGUACAGUUCUAGUGUCUAAAACC^G-5' (SEQ ID NO: 549)

EGFR-2818 Target: 5'-AGCATGTCAAGATCACAGATTTTGGGC-3' (SEQ ID NO: 905)

5'-GCAUGUCAAGAUCACAGAUUUUGGG^A-3' (SEQ ID NO: 1974)
 3'-CGUACAGUUCUAGUGUCUAAAACCC^G-5' (SEQ ID NO: 550)

EGFR-2819 Target: 5'-GCATGTCAAGATCACAGATTTTGGGCT-3' (SEQ ID NO: 906)

5'-CAUGUCAAGAUCACAGAUUUUGGGC^A-3' (SEQ ID NO: 1975)
 3'-GUACAGUUCUAGUGUCUAAAACCCG^A-5' (SEQ ID NO: 551)

EGFR-2820 Target: 5'-CATGTCAAGATCACAGATTTTGGGCTG-3' (SEQ ID NO: 907)

5'-AUGUCAAGAUCACAGAUUUUGGGCU^A-3' (SEQ ID NO: 1976)
 3'-UACAGUUCUAGUGUCUAAAACCCGA^C-5' (SEQ ID NO: 552)

EGFR-2821 Target: 5'-ATGTCAAGATCACAGATTTTGGGCTGG-3' (SEQ ID NO: 908)

5'-UGUCAAGAUCACAGAUUUUGGGCUG^A-3' (SEQ ID NO: 1977)
 3'-ACAGUUCUAGUGUCUAAAACCCGAC_G-5' (SEQ ID NO: 553)

EGFR-2822 Target: 5'-TGTCAAGATCACAGATTTTGGGCTGGC-3' (SEQ ID NO: 909)

5'-GUCAAGAUCACAGAUUUUGGGCUGG^A-3' (SEQ ID NO: 1978)
 3'-CAGUUCUAGUGUCUAAAACCCGACC_G-5' (SEQ ID NO: 554)

EGFR-2823 Target: 5'-GTCAAGATCACAGATTTTGGGCTGGCC-3' (SEQ ID NO: 910)

5'-UCAAGAUCACAGAUUUUGGGCUGGC^A-3' (SEQ ID NO: 1979)
 3'-AGUUCUAGUGUCUAAAACCCGACCG_U-5' (SEQ ID NO: 555)

EGFR-2824 Target: 5'-TCAAGATCACAGATTTTGGGCTGGCCA-3' (SEQ ID NO: 911)

5'-CAAGAUCACAGAUUUUGGGCUGGCC^C-3' (SEQ ID NO: 1980)
 3'-GUUCUAGUGUCUAAAACCCGACCGG_U-5' (SEQ ID NO: 556)

EGFR-2825 Target: 5'-CAAGATCACAGATTTTGGGCTGGCCAA-3' (SEQ ID NO: 912)

5'-AAGAUCACAGAUUUUGGGCUGGCCA^C-3' (SEQ ID NO: 1981)
 3'-UUCUAGUGUCUAAAACCCGACCGGU_U-5' (SEQ ID NO: 557)

EGFR-2826 Target: 5'-AAGATCACAGATTTTGGGCTGGCCAAA-3' (SEQ ID NO: 913)

5'-AGAUCACAGAUUUUGGGCUGGCCAA^C-3' (SEQ ID NO: 1982)
 3'-UCUAGUGUCUAAAACCCGACCGGU_U-5' (SEQ ID NO: 558)

EGFR-2827 Target: 5'-AGATCACAGATTTTGGGCTGGCCAAAC-3' (SEQ ID NO: 914)

5'-GAUCACAGAUUUUGGGCUGGCCAAA^A-3' (SEQ ID NO: 1983)
 3'-CUAGUGUCUAAAACCCGACCGGUU_G-5' (SEQ ID NO: 559)

EGFR-2828 Target: 5'-GATCACAGATTTTGGGCTGGCCAAACT-3' (SEQ ID NO: 915)

5'-AUCACAGAUUUUGGGCUGGCCAAAC^A-3' (SEQ ID NO: 1984)
 3'-UAGUGUCUAAAACCCGACCGGUU_G-5' (SEQ ID NO: 560)

EGFR-2829 Target: 5'-ATCACAGATTTTGGGCTGGCCAAACTG-3' (SEQ ID NO: 916)

5'-UCACAGAUUUUGGGCUGGCCAAACU^A-3' (SEQ ID NO: 1985)
 3'-AGUGUCUAAAACCCGACCGGUUGA_C-5' (SEQ ID NO: 561)

EGFR-2830 Target: 5'-TCACAGATTTTGGGCTGGCCAAACTGC-3' (SEQ ID NO: 917)

5'-CACAGAUUUUGGGCUGGCCAAACUG^A-3' (SEQ ID NO: 1986)

3'-GUGUCUAAAACCCGACCGGUUUGAC_GA-5', (SEQ ID NO: 562)

EGFR-2831 Target: 5'-CACAGATTTTGGGCTGGCCAAACTGCT-3' (SEQ ID NO: 918)

5'-ACAGAUUUUUGGGCUGGCCAAACUGC^A-3' (SEQ ID NO: 1987)

3'-UGUCUAAAACCCGACCGGUUUGACG_AC-5', (SEQ ID NO: 563)

EGFR-2832 Target: 5'-ACAGATTTTGGGCTGGCCAAACTGCTG-3' (SEQ ID NO: 919)

5'-CAGAUUUUUGGGCUGGCCAAACUGCU^A-3' (SEQ ID NO: 1988)

3'-GUCUAAAACCCGACCGGUUUGACGA_C-5', (SEQ ID NO: 564)

EGFR-2833 Target: 5'-CAGATTTTGGGCTGGCCAAACTGCTGG-3' (SEQ ID NO: 920)

5'-AGAUUUUUGGGCUGGCCAAACUGCUG^A-3' (SEQ ID NO: 1989)

3'-UCUAAAACCCGACCGGUUUGACGAC_C-5', (SEQ ID NO: 565)

EGFR-2834 Target: 5'-AGATTTTGGGCTGGCCAAACTGCTGGG-3' (SEQ ID NO: 921)

5'-GAUUUUGGGCUGGCCAAACUGCUGG^AC-3' (SEQ ID NO: 1990)

3'-CUAAAACCCGACCGGUUUGACGACC_A-5', (SEQ ID NO: 566)

EGFR-2835 Target: 5'-GATTTTGGGCTGGCCAAACTGCTGGGT-3' (SEQ ID NO: 922)

5'-AUUUUUGGGCUGGCCAAACUGCUGGG^AC-3' (SEQ ID NO: 1991)

3'-UAAAACCCGACCGGUUUGACGACCC_A-5', (SEQ ID NO: 567)

EGFR-2836 Target: 5'-ATTTTGGGCTGGCCAAACTGCTGGGTG-3' (SEQ ID NO: 923)

5'-UUUUGGGCUGGCCAAACUGCUGGGU^A-3' (SEQ ID NO: 1992)

3'-AAAACCCGACCGGUUUGACGACCCA_G-5', (SEQ ID NO: 568)

EGFR-2837 Target: 5'-TTTGGGCTGGCCAAACTGCTGGGTGC-3' (SEQ ID NO: 924)

5'-AGGCAAAGUGCCUAUCAAGUGGAUG^A-3' (SEQ ID NO: 1993)

3'-UCCGUUUCACGGAUAGUUCACCUAC_G-5', (SEQ ID NO: 569)

EGFR-2891 Target: 5'-AGGCAAAGTGCCTATCAAGTGGATGGC-3' (SEQ ID NO: 925)

5'-GGCAAAGUGCCUAUCAAGUGGAUGG^AC-3' (SEQ ID NO: 1994)

3'-CCGUUUCACGGAUAGUUCACCUACC_GU-5', (SEQ ID NO: 570)

EGFR-2892 Target: 5'-GGCAAAGTGCCTATCAAGTGGATGGCA-3' (SEQ ID NO: 926)

5'-GCAAAGUGCCUAUCAAGUGGAUGGC^C-3' (SEQ ID NO: 1995)

3'-CGUUUCACGGAUAGUUCACCUACCG_UA-5', (SEQ ID NO: 571)

EGFR-2893 Target: 5'-GCAAAGTGCCTATCAAGTGGATGGCAT-3' (SEQ ID NO: 927)

5'-CAAAGUGCCUAUCAAGUGGAUGGCA^C-3' (SEQ ID NO: 1996)
 3'-GUUUCACGGAUAGUUCACCUACCGUA^A-5' (SEQ ID NO: 572)

EGFR-2894 Target: 5'-CAAAGTGCCTATCAAGTGGATGGCATT-3' (SEQ ID NO: 928)

5'-AAAGUGCCUAUCAAGUGGAUGGCAU^A-3' (SEQ ID NO: 1997)
 3'-UUUCACGGAUAGUUCACCUACCGUA^A-5' (SEQ ID NO: 573)

EGFR-2895 Target: 5'-AAAGTGCCTATCAAGTGGATGGCATTG-3' (SEQ ID NO: 929)

5'-AAGUGCCUAUCAAGUGGAUGGCAU^A-3' (SEQ ID NO: 1998)
 3'-UUCACGGAUAGUUCACCUACCGUA^A-5' (SEQ ID NO: 574)

EGFR-2896 Target: 5'-AAGTGCCTATCAAGTGGATGGCATTGG-3' (SEQ ID NO: 930)

5'-AGUGCCUAUCAAGUGGAUGGCAU^A-3' (SEQ ID NO: 1999)
 3'-UCACGGAUAGUUCACCUACCGUA^A-5' (SEQ ID NO: 575)

EGFR-2897 Target: 5'-AGTGCCTATCAAGTGGATGGCATTGGA-3' (SEQ ID NO: 931)

5'-GUACCAUCGAUGUCUACAUGAUCAU^A-3' (SEQ ID NO: 2000)
 3'-CAUGGUAGCUACAGAUGUACUAGUA^A-5' (SEQ ID NO: 576)

EGFR-3088 Target: 5'-GTACCATCGATGTCTACATGATCATGG-3' (SEQ ID NO: 932)

5'-UACCAUCGAUGUCUACAUGAUCAU^A-3' (SEQ ID NO: 2001)
 3'-AUGGUAGCUACAGAUGUACUAGUA^A-5' (SEQ ID NO: 577)

EGFR-3089 Target: 5'-TACCATCGATGTCTACATGATCATGGT-3' (SEQ ID NO: 933)

5'-ACCAUCGAUGUCUACAUGAUCAU^A-3' (SEQ ID NO: 2002)
 3'-UGGUAGCUACAGAUGUACUAGUA^A-5' (SEQ ID NO: 578)

EGFR-3090 Target: 5'-ACCATCGATGTCTACATGATCATGGTC-3' (SEQ ID NO: 934)

5'-CCAUCGAUGUCUACAUGAUCAU^A-3' (SEQ ID NO: 2003)
 3'-GGUAGCUACAGAUGUACUAGUA^A-5' (SEQ ID NO: 579)

EGFR-3091 Target: 5'-CCATCGATGTCTACATGATCATGGTCA-3' (SEQ ID NO: 935)

5'-CAUCGAUGUCUACAUGAUCAU^A-3' (SEQ ID NO: 2004)
 3'-GUAGCUACAGAUGUACUAGUA^A-5' (SEQ ID NO: 580)

EGFR-3092 Target: 5'-CATCGATGTCTACATGATCATGGTCAA-3' (SEQ ID NO: 936)

5'-AUCGAUGUCUACAUGAUCAU^A-3' (SEQ ID NO: 2005)
 3'-UAGCUACAGAUGUACUAGUA^A-5' (SEQ ID NO: 581)

EGFR-3093 Target: 5'-ATCGATGTCTACATGATCATGGTCAAG-3' (SEQ ID NO: 937)

5'-UCGAUGUCUACAUGAUCAUGGUCAA^AC-3' (SEQ ID NO: 2006)
 3'-AGCUACAGAUGUACUAGUACCAGUUC_A-5' (SEQ ID NO: 582)

EGFR-3094 Target: 5'-TCGATGTCTACATGATCATGGTCAAGT-3' (SEQ ID NO: 938)

5'-CGAUGUCUACAUGAUCAUGGUCAAAG^CA-3' (SEQ ID NO: 2007)
 3'-GCUACAGAUGUACUAGUACCAGUUC_AC-5' (SEQ ID NO: 583)

EGFR-3095 Target: 5'-CGATGTCTACATGATCATGGTCAAGTG-3' (SEQ ID NO: 939)

5'-GAUGUCUACAUGAUCAUGGUCAAAGU^AA-3' (SEQ ID NO: 2008)
 3'-CUACAGAUGUACUAGUACCAGUUC_GA-5' (SEQ ID NO: 584)

EGFR-3096 Target: 5'-GATGTCTACATGATCATGGTCAAGTGC-3' (SEQ ID NO: 940)

5'-AUGUCUACAUGAUCAUGGUCAAAGUG^AC-3' (SEQ ID NO: 2009)
 3'-UACAGAUGUACUAGUACCAGUUCAC_GA-5' (SEQ ID NO: 585)

EGFR-3097 Target: 5'-ATGTCTACATGATCATGGTCAAGTGCT-3' (SEQ ID NO: 941)

5'-UGUCUACAUGAUCAUGGUCAAAGUGC^CA-3' (SEQ ID NO: 2010)
 3'-ACAGAUGUACUAGUACCAGUUCACG_AC-5' (SEQ ID NO: 586)

EGFR-3098 Target: 5'-TGTCTACATGATCATGGTCAAGTGCTG-3' (SEQ ID NO: 942)

5'-GUCUACAUGAUCAUGGUCAAAGUGCU^AA-3' (SEQ ID NO: 2011)
 3'-CAGAUGUACUAGUACCAGUUCACG_CA-5' (SEQ ID NO: 587)

EGFR-3099 Target: 5'-GTCTACATGATCATGGTCAAGTGCTGG-3' (SEQ ID NO: 943)

5'-UCUACAUGAUCAUGGUCAAAGUGCUG^AC-3' (SEQ ID NO: 2012)
 3'-AGAUGUACUAGUACCAGUUCACGAC_U-5' (SEQ ID NO: 588)

EGFR-3100 Target: 5'-TCTACATGATCATGGTCAAGTGCTGGA-3' (SEQ ID NO: 944)

5'-CUACAUGAUCAUGGUCAAAGUGCUGG^CC-3' (SEQ ID NO: 2013)
 3'-GAUGUACUAGUACCAGUUCACGACC_UA-5' (SEQ ID NO: 589)

EGFR-3101 Target: 5'-CTACATGATCATGGTCAAGTGCTGGAT-3' (SEQ ID NO: 945)

5'-UACAUGAUCAUGGUCAAAGUGCUGGA^CA-3' (SEQ ID NO: 2014)
 3'-AUGUACUAGUACCAGUUCACGACCU_AC-5' (SEQ ID NO: 590)

EGFR-3102 Target: 5'-TACATGATCATGGTCAAGTGCTGGATG-3' (SEQ ID NO: 946)

5'-ACAUGAUCAUGGUCAAAGUGCUGGAU^AC-3' (SEQ ID NO: 2015)
 3'-UGUACUAGUACCAGUUCACGACCU_UA-5' (SEQ ID NO: 591)

EGFR-3103 Target: 5'-ACATGATCATGGTCAAGTGCTGGATGA-3' (SEQ ID NO: 947)

5'-CAUGAUC AUGGUCAAGUGCUGGAUG^C-3' (SEQ ID NO: 2016)
 3'-GUACUAGUACCAGUUCACGACCUAC^U_{A-5'} (SEQ ID NO: 592)

EGFR-3104 Target: 5'-CATGATCATGGTCAAGTGCTGGATGAT-3' (SEQ ID NO: 948)

5'-AUGAUC AUGGUCAAGUGCUGGAUGA^C-3' (SEQ ID NO: 2017)
 3'-UACUAGUACCAGUUCACGACCUACU^A_{U-5'} (SEQ ID NO: 593)

EGFR-3105 Target: 5'-ATGATCATGGTCAAGTGCTGGATGATA-3' (SEQ ID NO: 949)

5'-UGAUC AUGGUCAAGUGCUGGAUGAU^C_{A-3'} (SEQ ID NO: 2018)
 3'-ACUAGUACCAGUUCACGACCUACUA^U_{C-5'} (SEQ ID NO: 594)

EGFR-3106 Target: 5'-TGATCATGGTCAAGTGCTGGATGATAG-3' (SEQ ID NO: 950)

5'-GAUCAUGGUCAAGUGCUGGAUGAU^A_{C-3'} (SEQ ID NO: 2019)
 3'-CUAGUACCAGUUCACGACCUACUAU^U_{C-5'} (SEQ ID NO: 595)

EGFR-3107 Target: 5'-GATCATGGTCAAGTGCTGGATGATAGA-3' (SEQ ID NO: 951)

5'-AUCAUGGUCAAGUGCUGGAUGAUAG^C_{A-3'} (SEQ ID NO: 2020)
 3'-UAGUACCAGUUCACGACCUACUAUC^U_{G-5'} (SEQ ID NO: 596)

EGFR-3108 Target: 5'-ATCATGGTCAAGTGCTGGATGATAGAC-3' (SEQ ID NO: 952)

5'-UCAUGGUCAAGUGCUGGAUGAUAGA^A_{A-3'} (SEQ ID NO: 2021)
 3'-AGUACCAGUUCACGACCUACUAUCU^U_{G-5'} (SEQ ID NO: 597)

EGFR-3109 Target: 5'-TCATGGTCAAGTGCTGGATGATAGACG-3' (SEQ ID NO: 953)

5'-CAUGGUCAAGUGCUGGAUGAUAGAC^A_{A-3'} (SEQ ID NO: 2022)
 3'-GUACCAGUUCACGACCUACUAUCUG^C_{G-5'} (SEQ ID NO: 598)

EGFR-3110 Target: 5'-CATGGTCAAGTGCTGGATGATAGACGC-3' (SEQ ID NO: 954)

5'-AUGGUCAAGUGCUGGAUGAUAGACG^A_{C-3'} (SEQ ID NO: 2023)
 3'-UACCAGUUCACGACCUACUAUCUGC^G_{U-5'} (SEQ ID NO: 599)

EGFR-3111 Target: 5'-ATGGTCAAGTGCTGGATGATAGACGCA-3' (SEQ ID NO: 955)

5'-UGGUCAAGUGCUGGAUGAUAGACGC^A_{C-3'} (SEQ ID NO: 2024)
 3'-ACCAGUUCACGACCUACUAUCUGCG^U_{C-5'} (SEQ ID NO: 600)

EGFR-3112 Target: 5'-TGGTCAAGTGCTGGATGATAGACGCAG-3' (SEQ ID NO: 956)

5'-GGUCAAGUGCUGGAUGAUAGACGCA^A_{C-3'} (SEQ ID NO: 2025)

3'-CCAGUUCACGACCUACUAUCUGCGU_CU-5', (SEQ ID NO: 601)

EGFR-3113 Target: 5'-GGTCAAGTGCTGGATGATAGACGCAGA-3' (SEQ ID NO: 957)

5'-UCGAAUUCUCCAAAAUGGCCCCGAGA^A-3' (SEQ ID NO: 2026)

3'-AGCUUAAGAGGUUUUACCGGGCUCU_GG-5', (SEQ ID NO: 602)

EGFR-3169 Target: 5'-TCGAATTCTCCAAAAATGGCCCCGAGACC-3' (SEQ ID NO: 958)

5'-CGAAUUCUCCAAAAUGGCCCCGAGAC^A-3' (SEQ ID NO: 2027)

3'-GCUUAAGAGGUUUUACCGGGCUCUG_GG-5', (SEQ ID NO: 603)

EGFR-3170 Target: 5'-CGAATTCTCCAAAAATGGCCCCGAGACCC-3' (SEQ ID NO: 959)

5'-GGGAUGAAAGAAUGCAUUUGCCAAG^CA-3' (SEQ ID NO: 2028)

3'-CCCUACUUUCUUACGUAAACGGUUC_AG-5', (SEQ ID NO: 604)

EGFR-3220 Target: 5'-GGGATGAAAGAATGCATTTGCCAAGTC-3' (SEQ ID NO: 960)

5'-GGAUGAAAGAAUGCAUUUGCCAAGU^A-3' (SEQ ID NO: 2029)

3'-CCUACUUUCUUACGUAAACGGUUC_GG-5', (SEQ ID NO: 605)

EGFR-3221 Target: 5'-GGATGAAAGAATGCATTTGCCAAGTCC-3' (SEQ ID NO: 961)

5'-GAUGAAAGAAUGCAUUUGCCAAGUC^AC-3' (SEQ ID NO: 2030)

3'-CUACUUUCUUACGUAAACGGUUCAG_GA-5', (SEQ ID NO: 606)

EGFR-3222 Target: 5'-GATGAAAGAATGCATTTGCCAAGTCCT-3' (SEQ ID NO: 962)

5'-AUGAAAGAAUGCAUUUGCCAAGUCC^C-3' (SEQ ID NO: 2031)

3'-UACUUUCUUACGUAAACGGUUCAGG_AU-5', (SEQ ID NO: 607)

EGFR-3223 Target: 5'-ATGAAAGAATGCATTTGCCAAGTCCTA-3' (SEQ ID NO: 963)

5'-UGAAAGAAUGCAUUUGCCAAGUCCU^CA-3' (SEQ ID NO: 2032)

3'-ACUUUCUUACGUAAACGGUUCAGGA_UG-5', (SEQ ID NO: 608)

EGFR-3224 Target: 5'-TGAAAGAATGCATTTGCCAAGTCCTAC-3' (SEQ ID NO: 964)

5'-UGGACAACCCUGACUACCAGCAGGA^AC-3' (SEQ ID NO: 2033)

3'-ACCUGUUGGGACUGAUGGUCGUCCU_GA-5', (SEQ ID NO: 609)

EGFR-3772 Target: 5'-TGGACAACCCCTGACTACCAGCAGGACT-3' (SEQ ID NO: 965)

5'-GGACAACCCUGACUACCAGCAGGAC^C-3' (SEQ ID NO: 2034)

3'-CCUGUUGGGACUGAUGGUCGUCCUG_AA-5', (SEQ ID NO: 610)

EGFR-3773 Target: 5'-GGACAACCCCTGACTACCAGCAGGACTT-3' (SEQ ID NO: 966)

5'-GACAACCCUGACUACCAGCAGGACU^CA-3' (SEQ ID NO: 2035)
 3'-CUGUUGGGACUGAUGGUCGUCCUGA^AG-5' (SEQ ID NO: 611)

EGFR-3774 Target: 5'-GACAACCCCTGACTACCAGCAGGACTTC-3' (SEQ ID NO: 967)

5'-ACAACCCUGACUACCAGCAGGACUU^AC-3' (SEQ ID NO: 2036)
 3'-UGUUGGGACUGAUGGUCGUCCUGAA^GA-5' (SEQ ID NO: 612)

EGFR-3775 Target: 5'-ACAACCCCTGACTACCAGCAGGACTTCT-3' (SEQ ID NO: 968)

5'-CAACCCUGACUACCAGCAGGACUUC^CC-3' (SEQ ID NO: 2037)
 3'-GUUGGGACUGAUGGUCGUCCUGAAG^AA-5' (SEQ ID NO: 613)

EGFR-3776 Target: 5'-CAACCCCTGACTACCAGCAGGACTTCTT-3' (SEQ ID NO: 969)

5'-AACCCUGACUACCAGCAGGACUUCU^CC-3' (SEQ ID NO: 2038)
 3'-UUGGGACUGAUGGUCGUCCUGAAGA^AA-5' (SEQ ID NO: 614)

EGFR-3777 Target: 5'-AACCCCTGACTACCAGCAGGACTTCTTT-3' (SEQ ID NO: 970)

5'-ACCCUGACUACCAGCAGGACUUCUU^CA-3' (SEQ ID NO: 2039)
 3'-UGGGACUGAUGGUCGUCCUGAAGAA^AG-5' (SEQ ID NO: 615)

EGFR-3778 Target: 5'-ACCCTGACTACCAGCAGGACTTCTTTC-3' (SEQ ID NO: 971)

5'-CCCUGACUACCAGCAGGACUUCUUU^AA-3' (SEQ ID NO: 2040)
 3'-GGGACUGAUGGUCGUCCUGAAGAAA^GG-5' (SEQ ID NO: 616)

EGFR-3779 Target: 5'-CCCTGACTACCAGCAGGACTTCTTTCC-3' (SEQ ID NO: 972)

Table 8: Selected Mouse Anti-EGFR “Blunt/Fray” DsiRNAs

5'-CAGCGCAACGCGCAGCAGCCUCCCU^AA-3' (SEQ ID NO: 2041)
 3'-GUCGCGUUGCGCGUCGUCGGAGGGA^GG-5' (SEQ ID NO: 617)

EGFR-m71 Target: 5'-CAGCGCAACGCGCAGCAGCCTCCCTCC-3' (SEQ ID NO: 973)

5'-ACGCGCAGCAGCCUCCUCCUUCUUC^CC-3' (SEQ ID NO: 2042)
 3'-UGCGCGUCGUCGGAGGGAGGAGAAG^AA-5' (SEQ ID NO: 618)

EGFR-m78 Target: 5'-ACGCGCAGCAGCCTCCCTCCTTCTT-3' (SEQ ID NO: 974)

5'-AGCCUCCUCCUUCUUCUCCCGCAC^AA-3' (SEQ ID NO: 2043)
 3'-UCGGAGGGAGGAGAAGAAGGGCGUG^AC-5' (SEQ ID NO: 619)

EGFR-m87 Target: 5'-AGCCTCCCTCCTTCTTCTTCCCGCACTG-3' (SEQ ID NO: 975)

5'-CUCCCUCCUCUUCUCCCCGCACUGU^A-3' (SEQ ID NO: 2044)
3'-GAGGGAGGAGAAGAAGGGCGUGACA_G-5' (SEQ ID NO: 620)

EGFR-m90 Target: 5'-CTCCCTCTTCTTCTCCCGCACTGTGC-3' (SEQ ID NO: 976)

5'-CCCUCUCCUCUUCUCCCCGCACUGUGC^A-3' (SEQ ID NO: 2045)
3'-GGGAGGAGAAGAAGGGCGUGACACG_C-5' (SEQ ID NO: 621)

EGFR-m92 Target: 5'-CCCTCTCTTCTTCTCCCGCACTGTGCGC-3' (SEQ ID NO: 977)

5'-CUCCUCUUCUUCUCCCCGCACUGUGCGC^C-3' (SEQ ID NO: 2046)
3'-GAGGAGAAGAAGGGCGUGACACGCG_A-5' (SEQ ID NO: 622)

EGFR-m94 Target: 5'-CTCCTCTTCTTCCCGCACTGTGCGCTC-3' (SEQ ID NO: 978)

5'-CUCUUCUUCUCCCCGCACUGUGCGCUCC^C-3' (SEQ ID NO: 2047)
3'-GAGAAGAAGGGCGUGACACGCGAGG_A-5' (SEQ ID NO: 623)

EGFR-m97 Target: 5'-CTCTTCTTCCCGCACTGTGCGCTCCTC-3' (SEQ ID NO: 979)

5'-CUUCUUCUCCCCGCACUGUGCGCUCCUC^A-3' (SEQ ID NO: 2048)
3'-GAAGAAGGGCGUGACACGCGAGGAG_G-5' (SEQ ID NO: 624)

EGFR-m99 Target: 5'-CTTCTTCCCGCACTGTGCGCTCCTCCT-3' (SEQ ID NO: 980)

5'-UUCUUCUCCCCGCACUGUGCGCUCCUCC^C-3' (SEQ ID NO: 2049)
3'-AAGAAGGGCGUGACACGCGAGGAGG_A-5' (SEQ ID NO: 625)

EGFR-m100 Target: 5'-TTCTTCCCGCACTGTGCGCTCCTCCTG-3' (SEQ ID NO: 981)

5'-UCUUCUCCCCGCACUGUGCGCUCCUCCU^A-3' (SEQ ID NO: 2050)
3'-AGAAGGGCGUGACACGCGAGGAGGA_C-5' (SEQ ID NO: 626)

EGFR-m101 Target: 5'-TCTTCCCGCACTGTGCGCTCCTCCTGG-3' (SEQ ID NO: 982)

5'-CUGUGCGCUCCUCCUGGGCUAGGGC^A-3' (SEQ ID NO: 2051)
3'-GACACGCGAGGAGGACCCGAUCCCG_A-5' (SEQ ID NO: 627)

EGFR-m111 Target: 5'-CTGTGCGCTCCTCCTGGGCTAGGGCGT-3' (SEQ ID NO: 983)

5'-UGCGCUCCUCCUGGGCUAGGGCGUC^C-3' (SEQ ID NO: 2052)
3'-ACGCGAGGAGGACCCGAUCCCGCAG_A-5' (SEQ ID NO: 628)

EGFR-m114 Target: 5'-TGCGCTCCTCCTGGGCTAGGGCGTCTG-3' (SEQ ID NO: 984)

5'-CACACUGCUGGUGUUGCUGACCGCG^A-3' (SEQ ID NO: 2053)
3'-GUGUGACGACCACAACGACUGGCGC_G-5' (SEQ ID NO: 629)

EGFR-m333 Target: 5'-CACACTGCTGGTGTGCTGACCGCGCT-3' (SEQ ID NO: 985)

5'-ACACUGCUGGUGUUGCUGACCGCGC^A-3' (SEQ ID NO: 2054)
3'-UGUGACGACCACAACGACUGGCGCGA_G-5' (SEQ ID NO: 630)

EGFR-m334 Target: 5'-ACACTGCTGGTGTGCTGACCGCGCTC-3' (SEQ ID NO: 986)

5'-CACUGCUGGUGUUGCUGACCGCGCU^A-3' (SEQ ID NO: 2055)
3'-GUGACGACCACAACGACUGGCGCGA_G-5' (SEQ ID NO: 631)

EGFR-m335 Target: 5'-CACTGCTGGTGTGCTGACCGCGCTCT-3' (SEQ ID NO: 987)

5'-ACUGCUGGUGUUGCUGACCGCGCUC^A-3' (SEQ ID NO: 2056)
3'-UGACGACCACAACGACUGGCGCGAG_A-5' (SEQ ID NO: 632)

EGFR-m336 Target: 5'-ACTGCTGGTGTGCTGACCGCGCTCTG-3' (SEQ ID NO: 988)

5'-CUGCUGGUGUUGCUGACCGCGCUCU^A-3' (SEQ ID NO: 2057)
3'-GACGACCACAACGACUGGCGCGAGA_C-5' (SEQ ID NO: 633)

EGFR-m337 Target: 5'-CTGCTGGTGTGCTGACCGCGCTCTGC-3' (SEQ ID NO: 989)

5'-UGCUGGUGUUGCUGACCGCGCUCUG^A-3' (SEQ ID NO: 2058)
3'-ACGACCACAACGACUGGCGCGAGAC_G-5' (SEQ ID NO: 634)

EGFR-m338 Target: 5'-TGCTGGTGTGCTGACCGCGCTCTGCG-3' (SEQ ID NO: 990)

5'-GCUGGUGUUGCUGACCGCGCUCUGC^A-3' (SEQ ID NO: 2059)
3'-CGACCACAACGACUGGCGCGAGACG_C-5' (SEQ ID NO: 635)

EGFR-m339 Target: 5'-GCTGGTGTGCTGACCGCGCTCTGCGC-3' (SEQ ID NO: 991)

5'-UGGUGUUGCUGACCGCGCUCUGCGC^A-3' (SEQ ID NO: 2060)
3'-ACCACAACGACUGGCGCGAGACGCG_G-5' (SEQ ID NO: 636)

EGFR-m341 Target: 5'-TGGTGTGCTGACCGCGCTCTGCGCCG-3' (SEQ ID NO: 992)

5'-GGUGUUGCUGACCGCGCUCUGCGCC^A-3' (SEQ ID NO: 2061)
3'-CCACAACGACUGGCGCGAGACGCGG_C-5' (SEQ ID NO: 637)

EGFR-m342 Target: 5'-GGTGTGCTGACCGCGCTCTGCGCCGC-3' (SEQ ID NO: 993)

5'-GUGUUGCUGACCGCGCUCUGCGCCG^A-3' (SEQ ID NO: 2062)
3'-CACAACGACUGGCGCGAGACGCGGC_G-5' (SEQ ID NO: 638)

EGFR-m343 Target: 5'-GTGTTGCTGACCGCGCTCTGCGCCGCA-3' (SEQ ID NO: 994)

5'-UGUUGCUGACCGCGCUCUGCGCCGC^A-3' (SEQ ID NO: 2063)
3'-ACAACGACUGGCGCGAGACGCGCG_U-5' (SEQ ID NO: 639)

EGFR-m344 Target: 5'-TGTTGCTGACCGCGCTCTGCGCCGCAG-3' (SEQ ID NO: 995)

5'-UGCUGACCGCGCUCUGCGCCGCAGG^CA-3' (SEQ ID NO: 2064)
 3'-ACGACUGGCGCGAGACGCGGCGUCC^AC-5' (SEQ ID NO: 640)

EGFR-m347 Target: 5'-TGCTGACCGCGCTCTGCGCCGCAGGTG-3' (SEQ ID NO: 996)

5'-GCUGACCGCGCUCUGCGCCGCAGGU^AA-3' (SEQ ID NO: 2065)
 3'-CGACUGGCGCGAGACGCGGCGUCCA^CC-5' (SEQ ID NO: 641)

EGFR-m348 Target: 5'-GCTGACCGCGCTCTGCGCCGCAGGTGG-3' (SEQ ID NO: 997)

5'-UCCUGAUUGGUGCUGUGCGAUUCAG^AC-3' (SEQ ID NO: 2066)
 3'-AGGACUAACCACGACACGCUAAGUC^GU-5' (SEQ ID NO: 642)

EGFR-m734 Target: 5'-TCCTGATTGGTGCTGTGCGATTGAGCA-3' (SEQ ID NO: 998)

5'-CCUGAUUGGUGCUGUGCGAUUCAGC^CC-3' (SEQ ID NO: 2067)
 3'-GGACUAACCACGACACGCUAAGUCG^UU-5' (SEQ ID NO: 643)

EGFR-m735 Target: 5'-CCTGATTGGTGCTGTGCGATTGAGCAA-3' (SEQ ID NO: 999)

5'-CUGAUUGGUGCUGUGCGAUUCAGCA^AC-3' (SEQ ID NO: 2068)
 3'-GACUAACCACGACACGCUAAGUCGU^UG-5' (SEQ ID NO: 644)

EGFR-m736 Target: 5'-CTGATTGGTGCTGTGCGATTGAGCAAC-3' (SEQ ID NO: 1000)

5'-GAUUGGUGCUGUGCGAUUCAGCAAC^CC-3' (SEQ ID NO: 2069)
 3'-CUAACCACGACACGCUAAGUCGUUG^UU-5' (SEQ ID NO: 645)

EGFR-m738 Target: 5'-GATTGGTGCTGTGCGATTGAGCAACAA-3' (SEQ ID NO: 1001)

5'-UUGGUGCUGUGCGAUUCAGCAACAA^AA-3' (SEQ ID NO: 2070)
 3'-AACCACGACACGCUAAGUCGUUGU^UG_G-5' (SEQ ID NO: 646)

EGFR-m740 Target: 5'-TTGGTGCTGTGCGATTGAGCAACAACC-3' (SEQ ID NO: 1002)

5'-UGGUGCUGUGCGAUUCAGCAACAAC^AA-3' (SEQ ID NO: 2071)
 3'-ACCACGACACGCUAAGUCGUUGU^UG_G-5' (SEQ ID NO: 647)

EGFR-m741 Target: 5'-TGGTGCTGTGCGATTGAGCAACAACCC-3' (SEQ ID NO: 1003)

5'-UCCAAGCUGUCCCAAUGGAAGCUGC^AA-3' (SEQ ID NO: 2072)
 3'-AGGUUCGACAGGGUUAACCUUCGACG^AC-5' (SEQ ID NO: 648)

EGFR-m879 Target: 5'-TCCAAGCTGTCCCAATGGAAGCTGCTG-3' (SEQ ID NO: 1004)

5'-CUGUGCCCAGCAAUGUCCCAUCGC^AA-3' (SEQ ID NO: 2073)

3'-GACACGGGUCGUUACAAGGGUAGCG_AC-5', (SEQ ID NO: 649)

EGFR-m948 Target: 5'-CTGTGCCCAGCAATGTTCCCATCGCTG-3' (SEQ ID NO: 1005)

5'-GGAAGUACAGCUUUGGUGCCACCUG^CA-3' (SEQ ID NO: 2074)
3'-CCUUCAUGUCGAAACCACGGUGGAC_AC-5', (SEQ ID NO: 650)

EGFR-m1154 Target: 5'-GGAAGTACAGCTTTGGTGCCACCTGTG-3' (SEQ ID NO: 1006)

5'-CUGUCGCAAAGUUUGUAAUGGCAUA^AA-3' (SEQ ID NO: 2075)
3'-GACAGCGUUUCAAAACAUUACCGUAU_CC-5', (SEQ ID NO: 651)

EGFR-m1302 Target: 5'-CTGTCGCAAAGTTTGTAATGGCATAGG-3' (SEQ ID NO: 1007)

5'-GGGAUUCUUUCACGCGCACUCCUCC^CA-3' (SEQ ID NO: 2076)
3'-CCCUAAGAAAGUGCGCGUGAGGAGG_AG-5', (SEQ ID NO: 652)

EGFR-m1439 Target: 5'-GGGATTCTTTTACGCGCACTCCTCCTC-3' (SEQ ID NO: 1008)

5'-AACAGGCUUUUUGCUGAUUCAGGCU^CA-3' (SEQ ID NO: 2077)
3'-UUGUCCGAAAAACGACUAAGUCCGA_AC-5', (SEQ ID NO: 653)

EGFR-m1509 Target: 5'-AACAGGCTTTTTGCTGATTCAGGCTTG-3' (SEQ ID NO: 1009)

5'-UUCAGGCUUGGCCUGAUAAACUGGAC^CA-3' (SEQ ID NO: 2078)
3'-AAGUCCGAACCGGACUAUUGACCUG_AC-5', (SEQ ID NO: 654)

EGFR-m1526 Target: 5'-TTCAGGCTTGGCCTGATAACTGGACTG-3' (SEQ ID NO: 1010)

5'-CAGGCUUGGCCUGAUAAACUGGACUG^CA-3' (SEQ ID NO: 2079)
3'-GUCCGAACCGGACUAUUGACCUGAC_UG-5', (SEQ ID NO: 655)

EGFR-m1528 Target: 5'-CAGGCTTGGCCTGATAACTGGACTGAC-3' (SEQ ID NO: 1011)

5'-GCUUGGCCUGAUAAACUGGACUGACC^CA-3' (SEQ ID NO: 2080)
3'-CGAACCGGACUAUUGACCUGACUGG_AG-5', (SEQ ID NO: 656)

EGFR-m1531 Target: 5'-GCTTGGCCTGATAACTGGACTGACCTC-3' (SEQ ID NO: 1012)

5'-ACGCCAACUGUACCUAUGGAUGUGC^CA-3' (SEQ ID NO: 2081)
3'-UGCGGUUGACAUGGAUACCUACACG_AC-5', (SEQ ID NO: 657)

EGFR-m2168 Target: 5'-ACGCCAACTGTACCTATGGATGTGCTG-3' (SEQ ID NO: 1013)

5'-CACUGGGAUUGUGGGUGGCCUCCUC^CC-3' (SEQ ID NO: 2082)
3'-GUGACCCUAAACACCCACCGGAGGAG_AA-5', (SEQ ID NO: 658)

EGFR-m2253 Target: 5'-CACTGGGATTGTGGGTGGCCTCCTCTT-3' (SEQ ID NO: 1014)

5'-GGUGGUGGCCCCUUGGGAUUGGCCUA^C-3' (SEQ ID NO: 2083)
 3'-CCACCACCGGGAACCCUAACCGGAU^A-5' (SEQ ID NO: 659)

EGFR-m2286 Target: 5'-GGTGGTGGCCCTTGGGATTGGCCTATT-3' (SEQ ID NO: 1015)

5'-GAUUGGCCUAUUAUGCGAAGACGU^A-3' (SEQ ID NO: 2084)
 3'-CUAACCGGAUAAGUACGCUUCUGCA^G-5' (SEQ ID NO: 660)

EGFR-m2301 Target: 5'-GATTGGCCTATTTCATGCGAAGACGTCA-3' (SEQ ID NO: 1016)

5'-CGCCGCCUGCUUCAAGAGAGAGAGC^A-3' (SEQ ID NO: 2085)
 3'-GCGGCGGACGAAGUUCUCUCUCG^A-5' (SEQ ID NO: 661)

EGFR-m2350 Target: 5'-CGCCGCCTGCTTCAAGAGAGAGAGCTC-3' (SEQ ID NO: 1017)

5'-GCCGCCUGCUUCAAGAGAGAGAGCU^A-3' (SEQ ID NO: 2086)
 3'-CGGCGGACGAAGUUCUCUCUCG^A-5' (SEQ ID NO: 662)

EGFR-m2351 Target: 5'-GCCGCCTGCTTCAAGAGAGAGAGCTCG-3' (SEQ ID NO: 1018)

5'-CCGCCUGCUUCAAGAGAGAGAGCUC^A-3' (SEQ ID NO: 2087)
 3'-GGCGGACGAAGUUCUCUCUCGAG^C-5' (SEQ ID NO: 663)

EGFR-m2352 Target: 5'-CCGCCTGCTTCAAGAGAGAGAGCTCGT-3' (SEQ ID NO: 1019)

5'-GUGGACAACCCUCAUGUAUGCCGCC^A-3' (SEQ ID NO: 2088)
 3'-CACCUGUUGGGAGUACAUAACGGCGG^A-5' (SEQ ID NO: 664)

EGFR-m2617 Target: 5'-GTGGACAACCCCTCATGTATGCCGCCTC-3' (SEQ ID NO: 1020)

5'-UGUAUGCCGCCUCCUGGGCAUCUGU^A-3' (SEQ ID NO: 2089)
 3'-ACAUAACGGCGGAGGACCCGUAGACA^G-5' (SEQ ID NO: 665)

EGFR-m2631 Target: 5'-TGTATGCCGCCTCCTGGGCATCTGTCT-3' (SEQ ID NO: 1021)

5'-CAGCUCAUGCCCUACGGUUGCCUCC^A-3' (SEQ ID NO: 2090)
 3'-GUCGAGUACGGGAUGCCAACGGAGG^A-5' (SEQ ID NO: 666)

EGFR-m2683 Target: 5'-CAGCTCATGCCCTACGGTTGCCTCCTG-3' (SEQ ID NO: 1022)

5'-AGCUCAUGCCCUACGGUUGCCUCC^A-3' (SEQ ID NO: 2091)
 3'-UCGAGUACGGGAUGCCAACGGAGG^A-5' (SEQ ID NO: 667)

EGFR-m2684 Target: 5'-AGCTCATGCCCTACGGTTGCCTCCTGG-3' (SEQ ID NO: 1023)

5'-GAUCGGCGUUUGGUGCACCGUGACU^A-3' (SEQ ID NO: 2092)
 3'-CUAGCCGCAAACACGUGGCACUGA^A-5' (SEQ ID NO: 668)

EGFR-m2800 Target: 5'-GATCGGCGTTTGGTGCACCGTGACTTG-3' (SEQ ID NO: 1024)

5'-GCGUUUGGUGCACCGUGACUUGGCA^A-3' (SEQ ID NO: 2093)
 3'-CGCAAACACGUGGCACUGAACCGU_C-5' (SEQ ID NO: 669)

EGFR-m2805 Target: 5'-GCGTTTGGTGACCGTGACTTGGCAGC-3' (SEQ ID NO: 1025)

5'-UUGGGCUGGCCAAACUGCUUGGUGC^A-3' (SEQ ID NO: 2094)
 3'-AACCCGACCGGUUUGACGAACCACG_A-5' (SEQ ID NO: 670)

EGFR-m2879 Target: 5'-TTGGGCTGGCCAAACTGCTTGGTGCTG-3' (SEQ ID NO: 1026)

5'-UGGGCUGGCCAAACUGCUUGGUGCU^A-3' (SEQ ID NO: 2095)
 3'-ACCCGACCGGUUUGACGAACCACG_A-5' (SEQ ID NO: 671)

EGFR-m2880 Target: 5'-TGGGCTGGCCAAACTGCTTGGTGCTGA-3' (SEQ ID NO: 1027)

5'-GGCUGGCCAAACUGCUUGGUGCUGA^A-3' (SEQ ID NO: 2096)
 3'-CCGACCGGUUUGACGAACCACGACU_U-5' (SEQ ID NO: 672)

EGFR-m2882 Target: 5'-GGCTGGCCAAACTGCTTGGTGCTGAAG-3' (SEQ ID NO: 1028)

5'-GCUGGCCAAACUGCUUGGUGCUGAA^A-3' (SEQ ID NO: 2097)
 3'-CGACCGGUUUGACGAACCACGACU_U-5' (SEQ ID NO: 673)

EGFR-m2883 Target: 5'-GCTGGCCAAACTGCTTGGTGCTGAAGA-3' (SEQ ID NO: 1029)

5'-GUCAAGUGCUGGAUGAUAGAUGCUG^C-3' (SEQ ID NO: 2098)
 3'-CAGUUCACGACCUACUAUCUACGAC_U-5' (SEQ ID NO: 674)

EGFR-m3154 Target: 5'-GTCAAGTGCTGGATGATAGATGCTGAT-3' (SEQ ID NO: 1030)

5'-UCAAGUGCUGGAUGAUAGAUGCUGA^C-3' (SEQ ID NO: 2099)
 3'-AGUUCACGACCUACUAUCUACGAC_U-5' (SEQ ID NO: 675)

EGFR-m3155 Target: 5'-TCAAGTGCTGGATGATAGATGCTGATA-3' (SEQ ID NO: 1031)

5'-CAAGUGCUGGAUGAUAGAUGCUGAU^A-3' (SEQ ID NO: 2100)
 3'-GUUCACGACCUACUAUCUACGACU_A-5' (SEQ ID NO: 676)

EGFR-m3156 Target: 5'-CAAGTGCTGGATGATAGATGCTGATAG-3' (SEQ ID NO: 1032)

5'-AAGUGCUGGAUGAUAGAUGCUGAU^A-3' (SEQ ID NO: 2101)
 3'-UUCACGACCUACUAUCUACGACU_A-5' (SEQ ID NO: 677)

EGFR-m3157 Target: 5'-AAGTGCTGGATGATAGATGCTGATAGC-3' (SEQ ID NO: 1033)

5'-AGUGCUGGAUGAUAGAUGCUGAUAG^A-3' (SEQ ID NO: 2102)
 3'-UCACGACCUACUAUCUACGACU_A-5' (SEQ ID NO: 678)

EGFR-m3158 Target: 5'-AGTGCTGGATGATAGATGCTGATAGCC-3' (SEQ ID NO: 1034)

5'-GUGCUGGAUGAUAGAUGCUGAUAGC^A-3' (SEQ ID NO: 2103)
3'-CACGACCUACUAUCUACGACUAUCG_G-5' (SEQ ID NO: 679)

EGFR-m3159 Target: 5'-GTGCTGGATGATAGATGCTGATAGCCG-3' (SEQ ID NO: 1035)

5'-UGCUGGAUGAUAGAUGCUGAUAGCC^A-3' (SEQ ID NO: 2104)
3'-ACGACCUACUAUCUACGACUAUCGG_G-5' (SEQ ID NO: 680)

EGFR-m3160 Target: 5'-TGCTGGATGATAGATGCTGATAGCCGC-3' (SEQ ID NO: 1036)

5'-GCUGGAUGAUAGAUGCUGAUAGCCG^A-3' (SEQ ID NO: 2105)
3'-CGACCUACUAUCUACGACUAUCGGC_G-5' (SEQ ID NO: 681)

EGFR-m3161 Target: 5'-GCTGGATGATAGATGCTGATAGCCGCC-3' (SEQ ID NO: 1037)

5'-CUGGAUGAUAGAUGCUGAUAGCCGC^A-3' (SEQ ID NO: 2106)
3'-GACCUACUAUCUACGACUAUCGGCG_G-5' (SEQ ID NO: 682)

EGFR-m3162 Target: 5'-CTGGATGATAGATGCTGATAGCCGCCC-3' (SEQ ID NO: 1038)

5'-UGGAUGAUAGAUGCUGAUAGCCGCC^A-3' (SEQ ID NO: 2107)
3'-ACCUACUAUCUACGACUAUCGGCGG_U-5' (SEQ ID NO: 683)

EGFR-m3163 Target: 5'-TGGATGATAGATGCTGATAGCCGCCCA-3' (SEQ ID NO: 1039)

5'-AUGAUAGAUGCUGAUAGCCGCCCA^A-3' (SEQ ID NO: 2108)
3'-UACUAUCUACGACUAUCGGCGGGU_U-5' (SEQ ID NO: 684)

EGFR-m3166 Target: 5'-ATGATAGATGCTGATAGCCGCCCAAAG-3' (SEQ ID NO: 1040)

5'-GAUAGAUGCUGAUAGCCGCCCAAAG^C-3' (SEQ ID NO: 2109)
3'-CUAUCUACGACUAUCGGCGGGUUC_A-5' (SEQ ID NO: 685)

EGFR-m3168 Target: 5'-GATAGATGCTGATAGCCGCCCAAAGTT-3' (SEQ ID NO: 1041)

5'-GAGCUGCCGUGUCAAAAGAAGACGCC^C-3' (SEQ ID NO: 2110)
3'-CUCGACGGCACAGUUUCUUCUGCGG_A-5' (SEQ ID NO: 686)

EGFR-m3474 Target: 5'-GAGCTGCCGTGTCAAAGAAGACGCCTT-3' (SEQ ID NO: 1042)

5'-AGCUGCCGUGUCAAAAGAAGACGCCU^C-3' (SEQ ID NO: 2111)
3'-UCGACGGCACAGUUUCUUCUGCGGA_A-5' (SEQ ID NO: 687)

EGFR-m3475 Target: 5'-AGCTGCCGTGTCAAAGAAGACGCCTTC-3' (SEQ ID NO: 1043)

5'-AAGACGCCUUCUUGCAGCGGUACAG^A-3' (SEQ ID NO: 2112)

3'-UUCUGCGGAAGAACGUCGCCAUGUC_GA-5', (SEQ ID NO: 688)

EGFR-m3491 Target: 5'-AAGACGCCTTCTTGACGCGGTACAGCT-3' (SEQ ID NO: 1044)

5'-AGACGCCUUCUUGCAGCGGUACAGC^A-3' (SEQ ID NO: 2113)
 3'-UCUGCGGAAGAACGUCGCCAUGUCG_AG-5', (SEQ ID NO: 689)

EGFR-m3492 Target: 5'-AGACGCCTTCTTGACGCGGTACAGCTC-3' (SEQ ID NO: 1045)

5'-GACGCCUUCUUGCAGCGGUACAGCU^A-3' (SEQ ID NO: 2114)
 3'-CUGCGGAAGAACGUCGCCAUGUCGA_G-5', (SEQ ID NO: 690)

EGFR-m3493 Target: 5'-GACGCCTTCTTGACGCGGTACAGCTCC-3' (SEQ ID NO: 1046)

5'-ACGCCUUCUUGCAGCGGUACAGCUC^A-3' (SEQ ID NO: 2115)
 3'-UGC GGAAGAACGUCGCCAUGUCGAG_G-5', (SEQ ID NO: 691)

EGFR-m3494 Target: 5'-ACGCCTTCTTGACGCGGTACAGCTCCG-3' (SEQ ID NO: 1047)

5'-CGCCUUCUUGCAGCGGUACAGCUCC^A-3' (SEQ ID NO: 2116)
 3'-GCGGAAGAACGUCGCCAUGUCGAGG_C-5', (SEQ ID NO: 692)

EGFR-m3495 Target: 5'-CGCCTTCTTGACGCGGTACAGCTCCGA-3' (SEQ ID NO: 1048)

5'-GCCUUCUUGCAGCGGUACAGCUCCG^A-3' (SEQ ID NO: 2117)
 3'-CGGAAGAACGUCGCCAUGUCGAGGC_U-5', (SEQ ID NO: 693)

EGFR-m3496 Target: 5'-GCCTTCTTGACGCGGTACAGCTCCGAC-3' (SEQ ID NO: 1049)

5'-CCUUCUUGCAGCGGUACAGCUCCGA^A-3' (SEQ ID NO: 2118)
 3'-GGAAGAACGUCGCCAUGUCGAGGCU_G-5', (SEQ ID NO: 694)

EGFR-m3497 Target: 5'-CCTTCTTGACGCGGTACAGCTCCGACC-3' (SEQ ID NO: 1050)

5'-GACUGGCUUUAAAGCAUAACUCUGA^C-3' (SEQ ID NO: 2119)
 3'-CUGACCGAAAUUCGUUAUUGAGACU_A-5', (SEQ ID NO: 695)

EGFR-m4056 Target: 5'-GACTGGCTTTAAAGCATAACTCTGATG-3' (SEQ ID NO: 1051)

5'-AAGUGGGCCUCUCUCCUGAUGCACU^C-3' (SEQ ID NO: 2120)
 3'-UUCACCCGGAGAGAGGACUACGUGA_A-5', (SEQ ID NO: 696)

EGFR-m4103 Target: 5'-AAGTGGGCCTCTCTCCTGATGCACTTT-3' (SEQ ID NO: 1052)

5'-AGUGGGCCUCUCUCCUGAUGCACUU^C-3' (SEQ ID NO: 2121)
 3'-UCACCCGGAGAGAGGACUACGUGAA_A-5', (SEQ ID NO: 697)

EGFR-m4104 Target: 5'-AGTGGGCCTCTCTCCTGATGCACTTTG-3' (SEQ ID NO: 1053)

5'-GUGGGCCUCUCUCCUGAUGCACUUU^A-3' (SEQ ID NO: 2122)
 3'-CACCCGGAGAGAGGACUACGUGAAA_C-5' (SEQ ID NO: 698)

EGFR-m4105 Target: 5'-GTGGGCCTCTCTCCTGATGCACTTTGG-3' (SEQ ID NO: 1054)

5'-UGGGCCUCUCUCCUGAUGCACUUUG^A-3' (SEQ ID NO: 2123)
 3'-ACCCGGAGAGAGGACUACGUGAAAC_C-5' (SEQ ID NO: 699)

EGFR-m4106 Target: 5'-TGGGCCTCTCTCCTGATGCACTTTGGG-3' (SEQ ID NO: 1055)

5'-GCCUCUCUCCUGAUGCACUUUGGGA^C-3' (SEQ ID NO: 2124)
 3'-CGGAGAGAGGACUACGUGAAACCCU_U-5' (SEQ ID NO: 700)

EGFR-m4109 Target: 5'-GCCTCTCTCCTGATGCACTTTGGGAAG-3' (SEQ ID NO: 1056)

5'-GAUUGAUGCACUCUUGUAGUCUGGU^C-3' (SEQ ID NO: 2125)
 3'-CUAACUACGUGAGAACAUCAGACCA_U-5' (SEQ ID NO: 701)

EGFR-m4309 Target: 5'-GATTGATGCACTCTTGTAGTCTGGTAC-3' (SEQ ID NO: 1057)

5'-UAGACUCCUUCUAUGUUUUCUGUU^C-3' (SEQ ID NO: 2126)
 3'-AUCUGAAGGAAGAUACAAAAGACAA_A-5' (SEQ ID NO: 702)

EGFR-m4619 Target: 5'-TAGACTTCCTTCTATGTTTTCTGTTTC-3' (SEQ ID NO: 1058)

5'-CUUCUAUGUUUUCUGUUUCAUUGUU^C-3' (SEQ ID NO: 2127)
 3'-GAAGAUACAAAAGACAAAGUAACAA_A-5' (SEQ ID NO: 703)

EGFR-m4627 Target: 5'-CTTCTATGTTTTCTGTTTCATTGTTTT-3' (SEQ ID NO: 1059)

5'-UAUGUUUUUCUCCUGGUAAACUGC^C-3' (SEQ ID NO: 2128)
 3'-AUACAAAAGAAGGACCAUUUGACGU_U-5' (SEQ ID NO: 704)

EGFR-m5006 Target: 5'-TATGTTTTCTTCCTGGTAAACTGCAG-3' (SEQ ID NO: 1060)

5'-AUGUUUUUCUCCUGGUAAACUGCA^A-3' (SEQ ID NO: 2129)
 3'-UACAAAAGAAGGACCAUUUGACGU_C-5' (SEQ ID NO: 705)

EGFR-m5007 Target: 5'-ATGTTTTCTTCCTGGTAAACTGCAGC-3' (SEQ ID NO: 1061)

5'-UGUUUUUCUCCUGGUAAACUGCAG^A-3' (SEQ ID NO: 2130)
 3'-ACAAAAGAAGGACCAUUUGACGUC_G-5' (SEQ ID NO: 706)

EGFR-m5008 Target: 5'-TGTTTTCTTCCTGGTAAACTGCAGCC-3' (SEQ ID NO: 1062)

5'-UUUCUCCUGGUAAACUGCAGCCAA^C-3' (SEQ ID NO: 2131)
 3'-AAAGAAGGACCAUUUGACGUCGGUU_U-5' (SEQ ID NO: 707)

EGFR-m5012 Target: 5'-TTTCTTCCTGGTAAACTGCAGCCAAAC-3' (SEQ ID NO: 1063)

5'-UUCGAUCUCCUAAUGCUGUGACCC^C-3' (SEQ ID NO: 2132)
 3'-AAGCUAGAAGGAUUACGACACUGGG^A-5' (SEQ ID NO: 708)

EGFR-m5329 Target: 5'-TTCGATCTTCCTAATGCTGTGACCCTT-3' (SEQ ID NO: 1064)

5'-UCGAUCUCCUAAUGCUGUGACCCU^C-3' (SEQ ID NO: 2133)
 3'-AGCUAGAAGGAUUACGACACUGGG^A-5' (SEQ ID NO: 709)

EGFR-m5330 Target: 5'-TCGATCTTCCTAATGCTGTGACCCTTT-3' (SEQ ID NO: 1065)

5'-UUGUUGCUACUUAACUGUAAA^C-3' (SEQ ID NO: 2134)
 3'-AACACGAUGAAGUAUUGACAUUUA^A-5' (SEQ ID NO: 710)

EGFR-m5403 Target: 5'-TTGTTGCTACTTCATAACTGTAAATTT-3' (SEQ ID NO: 1066)

5'-GCUUGCAGCAUCCUCUGGUUCCUA^A-3' (SEQ ID NO: 2135)
 3'-CGAACGUCGUAGGAGACCAAAGGAU^U-5' (SEQ ID NO: 711)

EGFR-m5638 Target: 5'-GCTTGACAGCATCCTCTGGTTTCCTAAC-3' (SEQ ID NO: 1067)

5'-CGUUGCAAGCCACUCUAACUGUAGC^C-3' (SEQ ID NO: 2136)
 3'-GCAACGUUCGGUGAGAUUGACAUCG^U-5' (SEQ ID NO: 712)

EGFR-m5895 Target: 5'-CGTTGCAAGCCACTCTAACTGTAGCAA-3' (SEQ ID NO: 1068)

Table 9: Selected Human Anti-EGFR "Blunt/Blunt" DsiRNAs

5'-GGCGCAGCGCGGCCGCGAGCAGCCUCCG-3' (SEQ ID NO: 2137)
 3'-CCGCGUCGCGCCGGCGUCGUCGGAGGC-5' (SEQ ID NO: 357)

EGFR-31 Target: 5'-GGCGCAGCGCGGCCGCGAGCAGCCTCCG-3' (SEQ ID NO: 713)

5'-GCGCAGCGCGGCCGCGAGCAGCCUCCG-3' (SEQ ID NO: 2138)
 3'-CGCGUCGCGCCGGCGUCGUCGGAGGCG-5' (SEQ ID NO: 358)

EGFR-32 Target: 5'-GCGCAGCGCGGCCGCGAGCAGCCTCCG-3' (SEQ ID NO: 714)

5'-GCAGCGCGGCCGCGAGCAGCCUCCGCC-3' (SEQ ID NO: 2139)
 3'-CGUCGCGCCGGCGUCGUCGGAGGCGGG-5' (SEQ ID NO: 359)

EGFR-34 Target: 5'-GCAGCGCGGCCGCGAGCAGCCTCCGCC-3' (SEQ ID NO: 715)

5'-CAGCGCUCCUGGCGCUGGCGUCGCGC-3' (SEQ ID NO: 2140)
 3'-GUCGCGAGGACCGCGACGACCGAGCG-5' (SEQ ID NO: 360)

EGFR-298 Target: 5'-CAGCGCTCCTGGCGCTGCTGGCTGCGC-3' (SEQ ID NO: 716)

5'-GCGCUCCUGGCGCUGGCGUCGCGCUC-3' (SEQ ID NO: 2141)
 3'-CGCGAGGACCGCGACGACCGAGCGAG-5' (SEQ ID NO: 361)

EGFR-300 Target: 5'-GCGCTCCTGGCGCTGCTGGCTGCGCTC-3' (SEQ ID NO: 717)

5'-GCUCCUGGCGCUGCUGGCGCUCUG-3' (SEQ ID NO: 2142)

3'-CGAGGACCGCGACGACCGACGCGAGAC-5' (SEQ ID NO: 362)

EGFR-302 Target: 5'-GCTCCTGGCGCTGCTGGCTGCGCTCTG-3' (SEQ ID NO: 718)

5'-CAGUUGGGCACUUUUGAAGAUCAUUUU-3' (SEQ ID NO: 2143)

3'-GUCAACCCGUGAAAAACUUCUAGUAAAA-5' (SEQ ID NO: 363)

EGFR-390 Target: 5'-CAGTTGGGCACTTTTGAAGATCATTTT-3' (SEQ ID NO: 719)

5'-UGGGAAUUUGGAAAUUACCUAUGUGCA-3' (SEQ ID NO: 2144)

3'-ACCCUUAACCUUUAUUGGAUACACGU-5' (SEQ ID NO: 364)

EGFR-458 Target: 5'-TGGAATTTGAAATTACCTATGTGCA-3' (SEQ ID NO: 720)

5'-AAUUAUGAUCUUUCCUUCUUAAGACC-3' (SEQ ID NO: 2145)

3'-UUAUACUAGAAAGGAAGAAUUCUGG-5' (SEQ ID NO: 365)

EGFR-489 Target: 5'-AATTATGATCTTTCCTTCTTAAAGACC-3' (SEQ ID NO: 721)

5'-GUGGCUUGGUUAUGUCCUCAUUGCCCUC-3' (SEQ ID NO: 2146)

3'-CACCGACCAUACAGGAGUAACGGGAG-5' (SEQ ID NO: 366)

EGFR-525 Target: 5'-GTGGCTGGTTATGTCTCATTTGCCCTC-3' (SEQ ID NO: 722)

5'-UGCCCAUGAGAAAAUUUACAGGAAAUCC-3' (SEQ ID NO: 2147)

3'-ACGGGUACUCUUUAAAUGUCCUUUAGG-5' (SEQ ID NO: 367)

EGFR-676 Target: 5'-TGCCCATGAGAAATTTACAGGAAATCC-3' (SEQ ID NO: 723)

5'-CCUGCAUGGCGCCGUGCGGUUCAGCAA-3' (SEQ ID NO: 2148)

3'-GGACGUACCGCGGCACGCCAAGUCGUU-5' (SEQ ID NO: 368)

EGFR-701 Target: 5'-CCTGCATGGCGCCGTGCGGTTTACGCAA-3' (SEQ ID NO: 724)

5'-UGGCGCCGUGCGGUUCAGCAACAACCC-3' (SEQ ID NO: 2149)

3'-ACCGCGGCACGCCAAGUCGUUGUUGGG-5' (SEQ ID NO: 369)

EGFR-707 Target: 5'-TGGCGCCGTGCGGTTTACGCAACAACCC-3' (SEQ ID NO: 725)

5'-UGGCGCCGUGCGGUUCAGCAACAACCC-3' (SEQ ID NO: 2150)

3'-ACCGCGGCACGCCAAGUCGUUGUUGGG-5' (SEQ ID NO: 370)

EGFR-707 Target: 5'-TGGCGCCGTGCGGTTTACGCAACAACCC-3' (SEQ ID NO: 726)

5'-GCGCCGUGCGGUUCAGCAACAACCCUG-3' (SEQ ID NO: 2151)

3'-CGCGGCACGCCAAGUCGUUGUUGGGAC-5' (SEQ ID NO: 371)

EGFR-709 Target: 5'-GCGCCGTGCGGTTTACGCAACAACCCTG-3' (SEQ ID NO: 727)

5'-CGCCGUGCGGUUCAGCAACAACCCUGC-3' (SEQ ID NO: 2152)

3'-GCGGCACGCCAAGUCGUUGUUGGGACG-5' (SEQ ID NO: 372)

EGFR-710 Target: 5'-CGCCGTGCGGTTTACGCAACAACCCTGC-3' (SEQ ID NO: 728)

5'-CAGCUGCCAAAAGUGUGAUCCAAGCUG-3' (SEQ ID NO: 2153)

3'-GUCGACGGUUUUCACACUAGGUUCGAC-5' (SEQ ID NO: 373)

EGFR-827 Target: 5'-CAGCTGCCAAAAGTGTGATCCAAGCTG-3' (SEQ ID NO: 729)

5'-AUCUGUGCCCAGCAGUGCUCCGGGCGC-3' (SEQ ID NO: 2154)
3'-UAGACACGGGUCGUCACGAGGCCCGCG-5' (SEQ ID NO: 374)

EGFR-912 Target: 5'-ATCTGTGCCCAGCAGTGCTCCGGGCGC-3' (SEQ ID NO: 730)

5'-CUGUGCCCAGCAGUGCUCCGGGCGCUG-3' (SEQ ID NO: 2155)
3'-GACACGGGUCGUCACGAGGCCCGCGAC-5' (SEQ ID NO: 375)

EGFR-914 Target: 5'-CTGTGCCCAGCAGTGCTCCGGGCGCTG-3' (SEQ ID NO: 731)

5'-GUGCUCCGGGCGCUGCCGUGGCAAGUC-3' (SEQ ID NO: 2156)
3'-CACGAGGCCCGCGACGGCACCGUUCAG-5' (SEQ ID NO: 376)

EGFR-926 Target: 5'-GTGCTCCGGGCGCTGCCGTGGCAAGTC-3' (SEQ ID NO: 732)

5'-GAGAGCGACUGCCUGGUCUGCCGCAA-3' (SEQ ID NO: 2157)
3'-CUCUCGUGACGGACCAGACGGCGUUU-5' (SEQ ID NO: 377)

EGFR-1005 Target: 5'-GAGAGCGACTGCCTGGTCTGCCGCAA-3' (SEQ ID NO: 733)

5'-CUGCCUGGUCUGCCGCAAUUCGAGA-3' (SEQ ID NO: 2158)
3'-GACGGACCAGACGGCGUUUAAGGCUCU-5' (SEQ ID NO: 378)

EGFR-1013 Target: 5'-CTGCCTGGTCTGCCGCAAATTCGAGA-3' (SEQ ID NO: 734)

5'-GACAGAUACGGCUCGUGCGUCCGAGC-3' (SEQ ID NO: 2159)
3'-CUGUCUAGUGCCGAGCACGCAGGCUCG-5' (SEQ ID NO: 379)

EGFR-1175 Target: 5'-GACAGATCACGGCTCGTGCGTCCGAGC-3' (SEQ ID NO: 735)

5'-CCGCAAAGUGUGUAACGGAAUAGGUUAU-3' (SEQ ID NO: 2160)
3'-GGCGUUUCACACAUUGCCUUAUCCAUA-5' (SEQ ID NO: 380)

EGFR-1271 Target: 5'-CCGCAAAGTGTGTAACGGAATAGGTAT-3' (SEQ ID NO: 736)

5'-CGGAUAGGUUAUUGGUGAAUUUAAAGA-3' (SEQ ID NO: 2161)
3'-GCCUUAUCCAUAACCACUUAUUUUUCU-5' (SEQ ID NO: 381)

EGFR-1286 Target: 5'-CGGAATAGGTATTGGTGAATTTAAAGA-3' (SEQ ID NO: 737)

5'-CUACGAAUUAUAAACACUUAUAAACU-3' (SEQ ID NO: 2162)
3'-GAUGCUUAUAAUUGUGAAGUUUUUGA-5' (SEQ ID NO: 382)

EGFR-1330 Target: 5'-CTACGAATATTAAACACTTCAAAAAC-3' (SEQ ID NO: 738)

5'-CCACAGGAACUGGAUAUUCUGAAAACC-3' (SEQ ID NO: 2163)
3'-GGUGUCCUUGACCUAUAAGACUUUUGG-5' (SEQ ID NO: 383)

EGFR-1437 Target: 5'-CCACAGGAACCTGGATATTCTGAAAACC-3' (SEQ ID NO: 739)

5'-CACAGGGUUUUUGCUGAUUCAGGCUUG-3' (SEQ ID NO: 2164)
3'-GUGUCCCAAAAACGACUAAGUCCGAAC-5' (SEQ ID NO: 384)

EGFR-1475 Target: 5'-CACAGGGTTTTTGCTGATTCAGGCTTG-3' (SEQ ID NO: 740)

5'-UUCAGGAAACAAAAUUUGUGCUAUGC-3' (SEQ ID NO: 2165)

3'-AAGUCCUUUGUUUUUAAACACGAUACG-5' (SEQ ID NO: 385)
EGFR-1661 Target: 5'-TTCAGGAAACAAAAATTTGTGCTATGC-3' (SEQ ID NO: 741)

5'-GUGCUAUGCAAAUACAAUAAACUGGAA-3' (SEQ ID NO: 2166)
3'-CACGAUACGUUUUAUGUUUUAUUGACCUU-5' (SEQ ID NO: 386)
EGFR-1679 Target: 5'-GTGCTATGCAAATACAATAAACTGGAA-3' (SEQ ID NO: 742)

5'-CCGGUCAGAAAACCAAAUUAUAAGCA-3' (SEQ ID NO: 2167)
3'-GGCCAGUCUUUUGGUUUUAAUAUUCGU-5' (SEQ ID NO: 387)
EGFR-1723 Target: 5'-CCGGTCAGAAAACCAAAATTATAAGCA-3' (SEQ ID NO: 743)

5'-CUGCGUCUCUUGCCGGAAUGUCAGCCG-3' (SEQ ID NO: 2168)
3'-GACGCAGAGAACGGCCUACAGUCGGC-5' (SEQ ID NO: 388)
EGFR-1838 Target: 5'-CTGCGTCTCTTGCCGGAATGTCAGCCG-3' (SEQ ID NO: 744)

5'-GGGCCCUCUUCUUGCUGCUGGUGGUGG-3' (SEQ ID NO: 2169)
3'-CCCGGGAGGAGAACGACGACCACCACC-5' (SEQ ID NO: 389)
EGFR-2227 Target: 5'-GGGCCCTCCTCTTGCTGCTGGTGGTGG-3' (SEQ ID NO: 745)

5'-GGCCCUCUUCUUGCUGCUGGUGGUGGC-3' (SEQ ID NO: 2170)
3'-CCGGGAGGAGAACGACGACCACCACCG-5' (SEQ ID NO: 390)
EGFR-2228 Target: 5'-GGCCCTCCTCTTGCTGCTGGTGGTGGC-3' (SEQ ID NO: 746)

5'-CUCCUCUUGCUGCUGGUGGUGGCCCUG-3' (SEQ ID NO: 2171)
3'-GAGGAGAACGACGACCACCACCGGGAC-5' (SEQ ID NO: 391)
EGFR-2232 Target: 5'-CTCCTCTTGCTGCTGGTGGTGGCCCTG-3' (SEQ ID NO: 747)

5'-UCCUCUUGCUGCUGGUGGUGGCCCUGG-3' (SEQ ID NO: 2172)
3'-AGGAGAACGACGACCACCACCGGGACC-5' (SEQ ID NO: 392)
EGFR-2233 Target: 5'-TCCTCTTGCTGCTGGTGGTGGCCCTGG-3' (SEQ ID NO: 748)

5'-CGGAAGCGCACGCUGCGGAGGCUGCUG-3' (SEQ ID NO: 2173)
3'-GCCUUCGCGUGCGACGCCUCCGACGAC-5' (SEQ ID NO: 393)
EGFR-2295 Target: 5'-CGGAAGCGCACGCTGCGGAGGCTGCTG-3' (SEQ ID NO: 749)

5'-AAGCGCACGCUGCGGAGGCUGCUGCAG-3' (SEQ ID NO: 2174)
3'-UUCGCGUGCGACGCCUCCGACGACGUC-5' (SEQ ID NO: 394)
EGFR-2298 Target: 5'-AAGCGCACGCTGCGGAGGCTGCTGAG-3' (SEQ ID NO: 750)

5'-AACUGAAUUCAAAAAGAUCAAAGUGCU-3' (SEQ ID NO: 2175)
3'-UUGACUUAAGUUUUUCUAGUUUCACGA-5' (SEQ ID NO: 395)
EGFR-2399 Target: 5'-AACTGAATTCAAAAAGATCAAAGTGCT-3' (SEQ ID NO: 751)

5'-CAAAGUGCUGGGCUCCGGUGCGUUCGG-3' (SEQ ID NO: 2176)
3'-GUUUCACGACCCGAGGCCACGCAAGCC-5' (SEQ ID NO: 396)
EGFR-2417 Target: 5'-CAAAGTGCTGGGCTCCGGTGCGTTCGG-3' (SEQ ID NO: 752)

5'-AAGUGCUGGGCUCCGGUGCGUUCGGCA-3' (SEQ ID NO: 2177)
3'-UUCACGACCCGAGGCCACGCAAGCCGU-5' (SEQ ID NO: 397)
EGFR-2419 Target: 5'-AAGTGCTGGGCTCCGGTTCGTTCGGCA-3' (SEQ ID NO: 753)

5'-AGUGCUGGGCUCCGGUGCGUUCGGCAC-3' (SEQ ID NO: 2178)
3'-UCACGACCCGAGGCCACGCAAGCCGUG-5' (SEQ ID NO: 398)
EGFR-2420 Target: 5'-AGTGCTGGGCTCCGGTTCGTTCGGCAC-3' (SEQ ID NO: 754)

5'-GUGCUGGGCUCCGGUGCGUUCGGCACG-3' (SEQ ID NO: 2179)
3'-CACGACCCGAGGCCACGCAAGCCGUGC-5' (SEQ ID NO: 399)
EGFR-2421 Target: 5'-GTGCTGGGCTCCGGTTCGTTCGGCACG-3' (SEQ ID NO: 755)

5'-UGCUGGGCUCCGGUGCGUUCGGCACGG-3' (SEQ ID NO: 2180)
3'-ACGACCCGAGGCCACGCAAGCCGUGCC-5' (SEQ ID NO: 400)
EGFR-2422 Target: 5'-TGCTGGGCTCCGGTTCGTTCGGCACGG-3' (SEQ ID NO: 756)

5'-CGUGUGCCGCCUGCUGGGCAUCUGCCU-3' (SEQ ID NO: 2181)
3'-GCACACGGCGGACGACCCGUAGACGGA-5' (SEQ ID NO: 401)
EGFR-2591 Target: 5'-CGTGTGCCGCTGCTGGGCATCTGCCT-3' (SEQ ID NO: 757)

5'-GUGUGCCGCCUGCUGGGCAUCUGCCUC-3' (SEQ ID NO: 2182)
3'-CACACGGCGGACGACCCGUAGACGGAG-5' (SEQ ID NO: 402)
EGFR-2592 Target: 5'-GTGTGCCGCTGCTGGGCATCTGCCTC-3' (SEQ ID NO: 758)

5'-GUGCCGCCUGCUGGGCAUCUGCCUCAC-3' (SEQ ID NO: 2183)
3'-CACGGCGGACGACCCGUAGACGGAGUG-5' (SEQ ID NO: 403)
EGFR-2594 Target: 5'-GTGCCGCTGCTGGGCATCTGCCTCAC-3' (SEQ ID NO: 759)

5'-CACCGUGCAGCUCAUCACGCAGCUCAU-3' (SEQ ID NO: 2184)
3'-GUGGCACGUCGAGUAGUGCGUCGAGUA-5' (SEQ ID NO: 404)
EGFR-2624 Target: 5'-CACCGTGCAGCTCATCACGCAGCTCAT-3' (SEQ ID NO: 760)

5'-CGUGCAGCUCAUCACGCAGCUCAUGCC-3' (SEQ ID NO: 2185)
3'-GCACGUCGAGUAGUGCGUCGAGUACGG-5' (SEQ ID NO: 405)
EGFR-2627 Target: 5'-CGTGCAGCTCATCACGCAGCTCATGCC-3' (SEQ ID NO: 761)

5'-CAGCUCAUCACGCAGCUCAUGCCCUUC-3' (SEQ ID NO: 2186)
3'-GUCGAGUAGUGCGUCGAGUACGGGAAG-5' (SEQ ID NO: 406)
EGFR-2631 Target: 5'-CAGCTCATCACGCAGCTCATGCCCTTC-3' (SEQ ID NO: 762)

5'-AGCUCAUCACGCAGCUCAUGCCCUUCG-3' (SEQ ID NO: 2187)
3'-UCGAGUAGUGCGUCGAGUACGGGAAGC-5' (SEQ ID NO: 407)
EGFR-2632 Target: 5'-AGCTCATCACGCAGCTCATGCCCTTCG-3' (SEQ ID NO: 763)

5'-CAGCUCAUGCCCUUCGGCUGCCUCCUG-3' (SEQ ID NO: 2188)
3'-GUCGAGUACGGGAAGCCGACGGAGGAC-5' (SEQ ID NO: 408)
EGFR-2643 Target: 5'-CAGCTCATGCCCTTCGGCTGCCTCCTG-3' (SEQ ID NO: 764)

5'-AGCUCAUGCCCUUCGGCUGCCUCCUGG-3' (SEQ ID NO: 2189)
3'-UCGAGUACGGGAAGCCGACGGAGGACC-5' (SEQ ID NO: 409)
EGFR-2644 Target: 5'-AGCTCATGCCCTTCGGCTGCCTCCTGG-3' (SEQ ID NO: 765)

5'-UUGGAGGACCGUCGCUUGGUGCACC GC-3' (SEQ ID NO: 2190)
3'-AACCUCUGGCAGCGAACCACGUGGCG-5' (SEQ ID NO: 410)
EGFR-2754 Target: 5'-TTGGAGGACCGTCGCTTGGTGCACC GC-3' (SEQ ID NO: 766)

5'-GGAGGACCGUCGCUUGGUGCACC GC-3' (SEQ ID NO: 2191)
3'-CCUCCUGGCAGCGAACCACGUGGCGCU-5' (SEQ ID NO: 411)
EGFR-2756 Target: 5'-GGAGGACCGTCGCTTGGTGCACC GC-3' (SEQ ID NO: 767)

5'-GAGGACCGUCGCUUGGUGCACC GC-3' (SEQ ID NO: 2192)
3'-CUCCUGGCAGCGAACCACGUGGCGCUG-5' (SEQ ID NO: 412)
EGFR-2757 Target: 5'-GAGGACCGTCGCTTGGTGCACC GC-3' (SEQ ID NO: 768)

5'-AGGACCGUCGCUUGGUGCACC GC-3' (SEQ ID NO: 2193)
3'-UCCUGGCAGCGAACCACGUGGCGCUGG-5' (SEQ ID NO: 413)
EGFR-2758 Target: 5'-AGGACCGTCGCTTGGTGCACC GC-3' (SEQ ID NO: 769)

5'-GACCGUCGCUUGGUGCACC GC-3' (SEQ ID NO: 2194)
3'-CUGGCAGCGAACCACGUGGCGCUGGAC-5' (SEQ ID NO: 414)
EGFR-2760 Target: 5'-GACCGTCGCTTGGTGCACC GC-3' (SEQ ID NO: 770)

5'-CCGUCGCUUGGUGCACC GC-3' (SEQ ID NO: 2195)
3'-GGCAGCGAACCACGUGGCGCUGGACCG-5' (SEQ ID NO: 415)
EGFR-2762 Target: 5'-CCGTCGCTTGGTGCACC GC-3' (SEQ ID NO: 771)

5'-GUCGCUUGGUGCACC GC-3' (SEQ ID NO: 2196)
3'-CAGCGAACCACGUGGCGCUGGACCGUC-5' (SEQ ID NO: 416)
EGFR-2764 Target: 5'-GTCGCTTGGTGCACC GC-3' (SEQ ID NO: 772)

5'-UCGCUUGGUGCACC GC-3' (SEQ ID NO: 2197)
3'-AGCGAACCACGUGGCGCUGGACCGUCG-5' (SEQ ID NO: 417)
EGFR-2765 Target: 5'-TCGCTTGGTGCACC GC-3' (SEQ ID NO: 773)

5'-GCUUGGUGCACC GC-3' (SEQ ID NO: 2198)
3'-CGAACCACGUGGCGCUGGACCGUCGGU-5' (SEQ ID NO: 418)
EGFR-2767 Target: 5'-GCTTGGTGCACC GC-3' (SEQ ID NO: 774)

5'-GGCAUUGGAAUCAUUUUACACAGAAU-3' (SEQ ID NO: 2199)
3'-CCGUAACCUUAGUUAUUUUUGUGUCUUA-5' (SEQ ID NO: 419)
EGFR-2915 Target: 5'-GGCATTGGAATCAATTTTACACAGAAT-3' (SEQ ID NO: 775)

5'-UCAAGUGCUGGAUGAUAGACGCAGAU-3' (SEQ ID NO: 2200)
3'-AGUUCACGACCUACUAUCUGCGUCUAU-5' (SEQ ID NO: 420)

EGFR-3115 Target: 5'-TCAAGTGCTGGATGATAGACGCAGATA-3' (SEQ ID NO: 776)

5'-AAGUGCUGGAUGAUAGACGCAGAUAGU-3' (SEQ ID NO: 2201)

3'-UUCACGACCUACUAUCUGCGUCUAUCA-5' (SEQ ID NO: 421)

EGFR-3117 Target: 5'-AAGTGCTGGATGATAGACGCAGATAGT-3' (SEQ ID NO: 777)

5'-AGUGCUGGAUGAUAGACGCAGAUAGUC-3' (SEQ ID NO: 2202)

3'-UCACGACCUACUAUCUGCGUCUAUCAG-5' (SEQ ID NO: 422)

EGFR-3118 Target: 5'-AGTGCTGGATGATAGACGCAGATAGTC-3' (SEQ ID NO: 778)

5'-UGCUGGAUGAUAGACGCAGAUAGUCGC-3' (SEQ ID NO: 2203)

3'-ACGACCUACUAUCUGCGUCUAUCAGCG-5' (SEQ ID NO: 423)

EGFR-3120 Target: 5'-TGCTGGATGATAGACGCAGATAGTCGC-3' (SEQ ID NO: 779)

5'-CUCCUGAGCUCUCUGAGUGCAACCAGC-3' (SEQ ID NO: 2204)

3'-GAGGACUCGAGAGACUCACGUUGGUCG-5' (SEQ ID NO: 424)

EGFR-3372 Target: 5'-CTCCTGAGCTCTCTGAGTGCAACCAGC-3' (SEQ ID NO: 780)

5'-CUGAGCUCUCUGAGUGCAACCAGCAAC-3' (SEQ ID NO: 2205)

3'-GACUCGAGAGACUCACGUUGGUCGUUG-5' (SEQ ID NO: 425)

EGFR-3375 Target: 5'-CTGAGCTCTCTGAGTGCAACCAGCAAC-3' (SEQ ID NO: 781)

5'-AAGCUGUCCCAUCAAGGAAGACAGCUU-3' (SEQ ID NO: 2206)

3'-UUCGACAGGGUAGUUCUUCUGUCGAA-5' (SEQ ID NO: 426)

EGFR-3440 Target: 5'-AAGCTGTCCCATCAAGGAAGACAGCTT-3' (SEQ ID NO: 782)

5'-AGCUGUCCCAUCAAGGAAGACAGCUUC-3' (SEQ ID NO: 2207)

3'-UCGACAGGGUAGUUCUUCUGUCGAAG-5' (SEQ ID NO: 427)

EGFR-3441 Target: 5'-AGCTGTCCCATCAAGGAAGACAGCTTC-3' (SEQ ID NO: 783)

5'-AAGACAGCUUCUUGCAGCGAUACAGCU-3' (SEQ ID NO: 2208)

3'-UUCUGUCGAAGAACGUCGCUAUGUCGA-5' (SEQ ID NO: 428)

EGFR-3457 Target: 5'-AAGACAGCTTCTTGACGCGATACAGCT-3' (SEQ ID NO: 784)

5'-AGACAGCUUCUUGCAGCGAUACAGCUC-3' (SEQ ID NO: 2209)

3'-UCUGUCGAAGAACGUCGCUAUGUCGAG-5' (SEQ ID NO: 429)

EGFR-3458 Target: 5'-AGACAGCTTCTTGACGCGATACAGCTC-3' (SEQ ID NO: 785)

5'-GACAGCUUCUUGCAGCGAUACAGCUCA-3' (SEQ ID NO: 2210)

3'-CUGUCGAAGAACGUCGCUAUGUCGAGU-5' (SEQ ID NO: 430)

EGFR-3459 Target: 5'-GACAGCTTCTTGACGCGATACAGCTCA-3' (SEQ ID NO: 786)

5'-ACAGCUUCUUGCAGCGAUACAGCUCAG-3' (SEQ ID NO: 2211)

3'-UGUCGAAGAACGUCGCUAUGUCGAGUC-5' (SEQ ID NO: 431)

EGFR-3460 Target: 5'-ACAGCTTCTTGACGCGATACAGCTCAG-3' (SEQ ID NO: 787)

5'-CAGCUUCUUGCAGCGAUACAGCUCAGA-3' (SEQ ID NO: 2212)

3'-GUCGAAGAACGUCGCUAUGUCGAGUCU-5' (SEQ ID NO: 432)
EGFR-3461 Target: 5'-CAGCTTCTTGACGCGATACAGCTCAGA-3' (SEQ ID NO: 788)

5'-GCUUCUUGCAGCGAUACAGCUCAGACC-3' (SEQ ID NO: 2213)
3'-CGAAGAACGUCGCUAUGUCGAGUCUGG-5' (SEQ ID NO: 433)
EGFR-3463 Target: 5'-GCTTCTTGACGCGATACAGCTCAGACC-3' (SEQ ID NO: 789)

5'-CCACAAAGCAGUGAAUUUAUUGGAGCA-3' (SEQ ID NO: 2214)
3'-GGUGUUUCGUCACUAAAAUAACCUCGU-5' (SEQ ID NO: 434)
EGFR-3876 Target: 5'-CCACAAAGCAGTGAATTTATTGGAGCA-3' (SEQ ID NO: 790)

5'-GUAUAUUUGAAAAAAAAAAAAAGUAUA-3' (SEQ ID NO: 2215)
3'-CAUAUAAACUUUUUUUUUUUUUCAUAU-5' (SEQ ID NO: 435)
EGFR-4178 Target: 5'-GTATATTTGAAAAAAAAAAAAAGTATA-3' (SEQ ID NO: 791)

5'-UGUGAGGAUUUUUAUUGAUUGGGGAUC-3' (SEQ ID NO: 2216)
3'-ACACUCCUAAAAUAACUAACCCCUAG-5' (SEQ ID NO: 436)
EGFR-4205 Target: 5'-TGTGAGGATTTTTATTGATTGGGGATC-3' (SEQ ID NO: 792)

5'-CGCUAUUGAUUUUUACUUCAAUGGGCU-3' (SEQ ID NO: 2217)
3'-GCGAUAAACUAAAAUGAAGUUACCCGA-5' (SEQ ID NO: 437)
EGFR-4249 Target: 5'-CGCTATTGATTTTTACTTCAATGGGCT-3' (SEQ ID NO: 793)

5'-AAGGAAGAAGCUUGCUGGUAGCACUUG-3' (SEQ ID NO: 2218)
3'-UUCUUCUUCGAACGACCAUCGUGAAC-5' (SEQ ID NO: 438)
EGFR-4284 Target: 5'-AAGGAAGAAGCTTGCTGGTAGCACTTG-3' (SEQ ID NO: 794)

5'-AGGAAGAAGCUUGCUGGUAGCACUUGC-3' (SEQ ID NO: 2219)
3'-UCCUUCUUCGAACGACCAUCGUGAACG-5' (SEQ ID NO: 439)
EGFR-4285 Target: 5'-AGGAAGAAGCTTGCTGGTAGCACTTGC-3' (SEQ ID NO: 795)

5'-GGAAGAAGCUUGCUGGUAGCACUUGCU-3' (SEQ ID NO: 2220)
3'-CCUUCUUCGAACGACCAUCGUGAACGA-5' (SEQ ID NO: 440)
EGFR-4286 Target: 5'-GGAAGAAGCTTGCTGGTAGCACTTGCT-3' (SEQ ID NO: 796)

5'-GAAGAAGCUUGCUGGUAGCACUUGCUA-3' (SEQ ID NO: 2221)
3'-CUUCUUCGAACGACCAUCGUGAACGAU-5' (SEQ ID NO: 441)
EGFR-4287 Target: 5'-GAAGAAGCTTGCTGGTAGCACTTGCTA-3' (SEQ ID NO: 797)

5'-AAGAAGCUUGCUGGUAGCACUUGCUC-3' (SEQ ID NO: 2222)
3'-UUCUUCGAACGACCAUCGUGAACGAUG-5' (SEQ ID NO: 442)
EGFR-4288 Target: 5'-AAGAAGCTTGCTGGTAGCACTTGCTAC-3' (SEQ ID NO: 798)

5'-GAAGCUUGCUGGUAGCACUUGCUCACCC-3' (SEQ ID NO: 2223)
3'-CUUCGAACGACCAUCGUGAACGAUGGG-5' (SEQ ID NO: 443)
EGFR-4290 Target: 5'-GAAGCTTGCTGGTAGCACTTGCTACCC-3' (SEQ ID NO: 799)

5'-AAGCUUGCUGGUAGCACUUGCUACCCU-3' (SEQ ID NO: 2224)
3'-UUCGAACGACCAUCGUGAACGAUGGGA-5' (SEQ ID NO: 444)
EGFR-4291 Target: 5'-AAGCTTGCTGGTAGCACTTGCTACCCT-3' (SEQ ID NO: 800)

5'-AGCUUGCUGGUAGCACUUGCUACCCUG-3' (SEQ ID NO: 2225)
3'-UCGAACGACCAUCGUGAACGAUGGGAC-5' (SEQ ID NO: 445)
EGFR-4292 Target: 5'-AGCTTGCTGGTAGCACTTGCTACCCTG-3' (SEQ ID NO: 801)

5'-GCUUGCUGGUAGCACUUGCUACCCUGA-3' (SEQ ID NO: 2226)
3'-CGAACGACCAUCGUGAACGAUGGGACU-5' (SEQ ID NO: 446)
EGFR-4293 Target: 5'-GCTTGCTGGTAGCACTTGCTACCCTGA-3' (SEQ ID NO: 802)

5'-CUUGCUGGUAGCACUUGCUACCCUGAG-3' (SEQ ID NO: 2227)
3'-GAACGACCAUCGUGAACGAUGGGACUC-5' (SEQ ID NO: 447)
EGFR-4294 Target: 5'-CTTGCTGGTAGCACTTGCTACCCTGAG-3' (SEQ ID NO: 803)

5'-UUGCUGGUAGCACUUGCUACCCUGAGU-3' (SEQ ID NO: 2228)
3'-AACGACCAUCGUGAACGAUGGGACUCA-5' (SEQ ID NO: 448)
EGFR-4295 Target: 5'-TTGCTGGTAGCACTTGCTACCCTGAGT-3' (SEQ ID NO: 804)

5'-GGAUGCUUGAUUCCAGUGGUUCUGCUU-3' (SEQ ID NO: 2229)
3'-CCUACGAACUAAGGUCACCAAGACGAA-5' (SEQ ID NO: 449)
EGFR-4372 Target: 5'-GGATGCTTGATTCCAGTGGTTCTGCTT-3' (SEQ ID NO: 805)

5'-GAUGCUUGAUUCCAGUGGUUCUGCUUC-3' (SEQ ID NO: 2230)
3'-CUACGAACUAAGGUCACCAAGACGAAG-5' (SEQ ID NO: 450)
EGFR-4373 Target: 5'-GATGCTTGATTCCAGTGGTTCTGCTTC-3' (SEQ ID NO: 806)

5'-AGCAGGCCGGAUCGGUACUGUAUCAAG-3' (SEQ ID NO: 2231)
3'-UCGUCCGGCCUAGCCAUGACAUAGUUC-5' (SEQ ID NO: 451)
EGFR-4450 Target: 5'-AGCAGGCCGGATCGGTACTGTATCAAG-3' (SEQ ID NO: 807)

5'-GCCGGAUCGGUACUGUAUCAAGUCAUG-3' (SEQ ID NO: 2232)
3'-CGGCCUAGCCAUGACAUAGUUCAGUAC-5' (SEQ ID NO: 452)
EGFR-4455 Target: 5'-GCCGGATCGGTACTGTATCAAGTCATG-3' (SEQ ID NO: 808)

5'-UCCUUAGACUUACUUUUGUAAAAAUGU-3' (SEQ ID NO: 2233)
3'-AGGAAUCUGAAUGAAAACAUUUUUACA-5' (SEQ ID NO: 453)
EGFR-4550 Target: 5'-TCCTTAGACTTACTTTTGTAAAAATGT-3' (SEQ ID NO: 809)

5'-CUGUCUUGCUGUCAUGAAAUCAGCAAG-3' (SEQ ID NO: 2234)
3'-GACAGAACGACAGUACUUUAGUCGUUC-5' (SEQ ID NO: 454)
EGFR-4684 Target: 5'-CTGTCTTGCTGTCAATGAAATCAGCAAG-3' (SEQ ID NO: 810)

5'-CCUAAGGAUAGCACCGCUUUUGUUCUC-3' (SEQ ID NO: 2235)
3'-GGAUUCUAUCGUGGCGAAAACAAGAG-5' (SEQ ID NO: 455)
EGFR-4804 Target: 5'-CCTAAGGATAGCACCGCTTTTGTTC-3' (SEQ ID NO: 811)

5'-UAAGGAUAGCACCGCUUUUGUUCUCGC-3' (SEQ ID NO: 2236)
3'-AUUCCUAUCGUGGCGAAAACAAGAGCG-5' (SEQ ID NO: 456)
EGFR-4806 Target: 5'-TAAGGATAGCACCGCTTTTGTCTCTCGC-3' (SEQ ID NO: 812)

5'-AAGGAUAGCACCGCUUUUGUUCUCGCA-3' (SEQ ID NO: 2237)
3'-UUCCUAUCGUGGCGAAAACAAGAGCGU-5' (SEQ ID NO: 457)
EGFR-4807 Target: 5'-AAGGATAGCACCGCTTTTGTCTCTCGCA-3' (SEQ ID NO: 813)

5'-AGGAUAGCACCGCUUUUGUUCUCGCAA-3' (SEQ ID NO: 2238)
3'-UCCUAUCGUGGCGAAAACAAGAGCGUU-5' (SEQ ID NO: 458)
EGFR-4808 Target: 5'-AGGATAGCACCGCTTTTGTCTCTCGCAA-3' (SEQ ID NO: 814)

5'-GGAUAGCACCGCUUUUGUUCUCGCAAA-3' (SEQ ID NO: 2239)
3'-CCUAUCGUGGCGAAAACAAGAGCGUUU-5' (SEQ ID NO: 459)
EGFR-4809 Target: 5'-GGATAGCACCGCTTTTGTCTCTCGCAAA-3' (SEQ ID NO: 815)

5'-GAUAGCACCGCUUUUGUUCUCGCAAAA-3' (SEQ ID NO: 2240)
3'-CUAUCGUGGCGAAAACAAGAGCGUUUU-5' (SEQ ID NO: 460)
EGFR-4810 Target: 5'-GATAGCACCGCTTTTGTCTCTCGCAAAA-3' (SEQ ID NO: 816)

5'-AUAGCACCGCUUUUGUUCUCGCAAAAA-3' (SEQ ID NO: 2241)
3'-UAUCGUGGCGAAAACAAGAGCGUUUUU-5' (SEQ ID NO: 461)
EGFR-4811 Target: 5'-ATAGCACCGCTTTTGTCTCTCGCAAAAA-3' (SEQ ID NO: 817)

5'-UAGCACCGCUUUUGUUCUCGCAAAAAAC-3' (SEQ ID NO: 2242)
3'-AUCGUGGCGAAAACAAGAGCGUUUUUG-5' (SEQ ID NO: 462)
EGFR-4812 Target: 5'-TAGCACCGCTTTTGTCTCTCGCAAAAAAC-3' (SEQ ID NO: 818)

5'-AGCACCGCUUUUGUUCUCGCAAAAAACG-3' (SEQ ID NO: 2243)
3'-UCGUGGCGAAAACAAGAGCGUUUUUGC-5' (SEQ ID NO: 463)
EGFR-4813 Target: 5'-AGCACCGCTTTTGTCTCTCGCAAAAAACG-3' (SEQ ID NO: 819)

5'-ACCGCUUUUGUUCUCGCAAAAAACGUAU-3' (SEQ ID NO: 2244)
3'-UGGCGAAAACAAGAGCGUUUUUGCAUA-5' (SEQ ID NO: 464)
EGFR-4816 Target: 5'-ACCGCTTTTGTCTCTCGCAAAAAACGTAT-3' (SEQ ID NO: 820)

5'-CCGCUUUUGUUCUCGCAAAAAACGUUUC-3' (SEQ ID NO: 2245)
3'-GGCGAAAACAAGAGCGUUUUUGCAUAG-5' (SEQ ID NO: 465)
EGFR-4817 Target: 5'-CCGCTTTTGTCTCTCGCAAAAAACGTATC-3' (SEQ ID NO: 821)

5'-CGCUUUUGUUCUCGCAAAAAACGUUUCU-3' (SEQ ID NO: 2246)
3'-GCGAAAACAAGAGCGUUUUUGCAUAGA-5' (SEQ ID NO: 466)
EGFR-4818 Target: 5'-CGCTTTTGTCTCTCGCAAAAAACGTATCT-3' (SEQ ID NO: 822)

5'-GCUUUUGUUCUCGCAAAAAACGUUUCUC-3' (SEQ ID NO: 2247)
3'-CGAAAACAAGAGCGUUUUUGCAUAGAG-5' (SEQ ID NO: 467)

EGFR-4819 Target: 5'-GCTTTTGTTCCTCGCAAAAACGTATCTC-3' (SEQ ID NO: 823)

5'-UGUUCUCGCAAAAACGUAUCUCCUAAU-3' (SEQ ID NO: 2248)

3'-ACAAGAGCGUUUUUGCAUAGAGGAUUA-5' (SEQ ID NO: 468)

EGFR-4824 Target: 5'-TGTTCTCGCAAAAACGTATCTCCTAAT-3' (SEQ ID NO: 824)

5'-CAAAAUUAGUUUGUGUUACUUAUGGAA-3' (SEQ ID NO: 2249)

3'-GUUUUAAUCAAAACACAAUGAAUACCUU-5' (SEQ ID NO: 469)

EGFR-4953 Target: 5'-CAAAATTAGTTTGTGTTACTTATGGAA-3' (SEQ ID NO: 825)

5'-ACUUAUGGAAGAUAGUUUUCUCCUUUU-3' (SEQ ID NO: 2250)

3'-UGAAUACCUUCUAUCAAAGAGGAAAA-5' (SEQ ID NO: 470)

EGFR-4970 Target: 5'-ACTTATGGAAGATAGTTTTCTCCTTTT-3' (SEQ ID NO: 826)

5'-CUUCAAAAAGCUUUUUACUCAAGAGUA-3' (SEQ ID NO: 2251)

3'-GAAGUUUUCGAAAAAUGAGUUUCUCAU-5' (SEQ ID NO: 471)

EGFR-5003 Target: 5'-CTTCAAAAGCTTTTTACTCAAAGAGTA-3' (SEQ ID NO: 827)

5'-AAACUAGGGUUUGAAAUUGAUAAUGCU-3' (SEQ ID NO: 2252)

3'-UUUGAUCCCAAACUUUAACUAUUACGA-5' (SEQ ID NO: 472)

EGFR-5206 Target: 5'-AACTAGGGTTTGAAATTGATAATGCT-3' (SEQ ID NO: 828)

5'-CCUAAAAUAAUUCUCUACAAUUGGAA-3' (SEQ ID NO: 2253)

3'-GGAUUUUUAAUAAAGAGAUGUUAACCUU-5' (SEQ ID NO: 473)

EGFR-5275 Target: 5'-CCTAAAAATAATTTCTCTACAATTGGAA-3' (SEQ ID NO: 829)

5'-AACAGCAGUCCUUUGUAAACAGUGUUU-3' (SEQ ID NO: 2254)

3'-UUGUCGUCAGGAAACAUUUGUCACAAA-5' (SEQ ID NO: 474)

EGFR-5374 Target: 5'-AACAGCAGTCCTTTGTAAACAGTGTTT-3' (SEQ ID NO: 830)

5'-UCCAAUUUAUCAAGGAAGAAAUGGUUC-3' (SEQ ID NO: 2255)

3'-AGGUUAAAUAGUCCUUCUUUACCAAG-5' (SEQ ID NO: 475)

EGFR-5429 Target: 5'-TCCAATTTATCAAGGAAGAAATGGTTC-3' (SEQ ID NO: 831)

5'-CAUACAAA AUGUCCUUUUGCUUUUAA-3' (SEQ ID NO: 2256)

3'-GUAUGUUUACAAGGAAAACGAAAAUU-5' (SEQ ID NO: 476)

EGFR-5497 Target: 5'-CATACAAAATGTTCTTTTGCTTTTAA-3' (SEQ ID NO: 832)

5'-AUGUCCUUUUGCUUUUAAAGUAAUUU-3' (SEQ ID NO: 2257)

3'-UACAAGGAAAACGAAAAUUUCAUUAAA-5' (SEQ ID NO: 477)

EGFR-5505 Target: 5'-ATGTTCTTTTGCTTTTAAAGTAATTT-3' (SEQ ID NO: 833)

5'-UGUCCUUUUGCUUUUAAAGUAAUUU-3' (SEQ ID NO: 2258)

3'-ACAAGGAAAACGAAAAUUUCAUUAAA-5' (SEQ ID NO: 478)

EGFR-5506 Target: 5'-TGTTCTTTTGCTTTTAAAGTAATTTT-3' (SEQ ID NO: 834)

5'-UUUUGCUUUUAAAGUAAUUUUGACUC-3' (SEQ ID NO: 2259)

3'-AAAACGAAAAUUUCAUUAAAAACUGAG-5' (SEQ ID NO: 479)
EGFR-5512 Target: 5'-TTTTGCTTTTAAAGTAATTTTGACTC-3' (SEQ ID NO: 835)

5'-UUGUUAAGAAAGUAUUUGAUUUUUGUC-3' (SEQ ID NO: 2260)
3'-AACAAUUCUUUCAUAAACUAAAAACAG-5' (SEQ ID NO: 480)
EGFR-5565 Target: 5'-TTGTAAAGAAAGTATTTGATTTTGTGTC-3' (SEQ ID NO: 836)

5'-AUUUGGAAAUUACCUAUGUGCAGAGGA-3' (SEQ ID NO: 2261)
3'-UAAACCUUUAUGGAUACACGUCUCCU-5' (SEQ ID NO: 481)
EGFR-463 Target: 5'-ATTTGGAAATTACCTATGTGCAGAGGA-3' (SEQ ID NO: 837)

5'-UUUGGAAAUUACCUAUGUGCAGAGGAA-3' (SEQ ID NO: 2262)
3'-AAACCUUUAUGGAUACACGUCUCCU-5' (SEQ ID NO: 482)
EGFR-464 Target: 5'-TTTGGAAATTACCTATGTGCAGAGGAA-3' (SEQ ID NO: 838)

5'-AUCUUUCCUUCUUAAGACCAUCCAGG-3' (SEQ ID NO: 2263)
3'-UAGAAAGGAAGAAUUUCUGGUAGGUCC-5' (SEQ ID NO: 483)
EGFR-496 Target: 5'-ATCTTTCCTTCTTAAAGACCATCCAGG-3' (SEQ ID NO: 839)

5'-UCUUUCCUUCUUAAGACCAUCCAGGA-3' (SEQ ID NO: 2264)
3'-AGAAAGGAAGAAUUUCUGGUAGGUCCU-5' (SEQ ID NO: 484)
EGFR-497 Target: 5'-TCTTTCCTTCTTAAAGACCATCCAGGA-3' (SEQ ID NO: 840)

5'-CUUUCUUCUUAAGACCAUCCAGGAG-3' (SEQ ID NO: 2265)
3'-GAAAGGAAGAAUUUCUGGUAGGUCCUC-5' (SEQ ID NO: 485)
EGFR-498 Target: 5'-CTTTCCTTCTTAAAGACCATCCAGGAG-3' (SEQ ID NO: 841)

5'-UUUCCUUCUUAAGACCAUCCAGGAGG-3' (SEQ ID NO: 2266)
3'-AAAGGAAGAAUUUCUGGUAGGUCCUCC-5' (SEQ ID NO: 486)
EGFR-499 Target: 5'-TTTCCTTCTTAAAGACCATCCAGGAGG-3' (SEQ ID NO: 842)

5'-UUCUUCUUAAGACCAUCCAGGAGGU-3' (SEQ ID NO: 2267)
3'-AAGGAAGAAUUUCUGGUAGGUCCUCCA-5' (SEQ ID NO: 487)
EGFR-500 Target: 5'-TTCCTTCTTAAAGACCATCCAGGAGGT-3' (SEQ ID NO: 843)

5'-UCCUUCUUAAGACCAUCCAGGAGGUG-3' (SEQ ID NO: 2268)
3'-AGGAAGAAUUUCUGGUAGGUCCUCCAC-5' (SEQ ID NO: 488)
EGFR-501 Target: 5'-TCCTTCTTAAAGACCATCCAGGAGGTG-3' (SEQ ID NO: 844)

5'-CCUUCUUAAGACCAUCCAGGAGGUGG-3' (SEQ ID NO: 2269)
3'-GGAAGAAUUUCUGGUAGGUCCUCCACC-5' (SEQ ID NO: 489)
EGFR-502 Target: 5'-CCTTCTTAAAGACCATCCAGGAGGTGG-3' (SEQ ID NO: 845)

5'-CUUCUUAAGACCAUCCAGGAGGUGGC-3' (SEQ ID NO: 2270)
3'-GAAGAAUUUCUGGUAGGUCCUCCACCG-5' (SEQ ID NO: 490)
EGFR-503 Target: 5'-CTTCTTAAAGACCATCCAGGAGGTGGC-3' (SEQ ID NO: 846)

5'-UUCUUAAGACCAUCCAGGAGGUGGCU-3' (SEQ ID NO: 2271)
3'-AAGAAUUCUGGUAGGUCCUCCACCGA-5' (SEQ ID NO: 491)

EGFR-504 Target: 5'-TTCTTAAAGACCATCCAGGAGGTGGCT-3' (SEQ ID NO: 847)

5'-UCUUAAGACCAUCCAGGAGGUGGCU-3' (SEQ ID NO: 2272)
3'-AGAAUUCUGGUAGGUCCUCCACCGAC-5' (SEQ ID NO: 492)

EGFR-505 Target: 5'-TCTTAAAGACCATCCAGGAGGTGGCTG-3' (SEQ ID NO: 848)

5'-CUUAAAGACCAUCCAGGAGGUGGCU-3' (SEQ ID NO: 2273)
3'-GAAUUCUGGUAGGUCCUCCACCGACC-5' (SEQ ID NO: 493)

EGFR-506 Target: 5'-CTTAAAGACCATCCAGGAGGTGGCTGG-3' (SEQ ID NO: 849)

5'-UUAAGACCAUCCAGGAGGUGGCU-3' (SEQ ID NO: 2274)
3'-AAUUCUGGUAGGUCCUCCACCGACCA-5' (SEQ ID NO: 494)

EGFR-507 Target: 5'-TTAAAGACCATCCAGGAGGTGGCTGGT-3' (SEQ ID NO: 850)

5'-UAAAGACCAUCCAGGAGGUGGCU-3' (SEQ ID NO: 2275)
3'-AUUUCUGGUAGGUCCUCCACCGACCAA-5' (SEQ ID NO: 495)

EGFR-508 Target: 5'-TAAAGACCATCCAGGAGGTGGCTGGTT-3' (SEQ ID NO: 851)

5'-AAAGACCAUCCAGGAGGUGGCU-3' (SEQ ID NO: 2276)
3'-UUUCUGGUAGGUCCUCCACCGACCAAU-5' (SEQ ID NO: 496)

EGFR-509 Target: 5'-AAAGACCATCCAGGAGGTGGCTGGTTA-3' (SEQ ID NO: 852)

5'-AGUGUGAUCCAAGCUGUCCCAAUGGGA-3' (SEQ ID NO: 2277)
3'-UCACACUAGGUUCGACAGGGUUACCCU-5' (SEQ ID NO: 497)

EGFR-838 Target: 5'-AGTGTGATCCAAGCTGTCCCAATGGGA-3' (SEQ ID NO: 853)

5'-GUGUGAUCCAAGCUGUCCCAAUGGGAG-3' (SEQ ID NO: 2278)
3'-CACACUAGGUUCGACAGGGUUACCCUC-5' (SEQ ID NO: 498)

EGFR-839 Target: 5'-GTGTGATCCAAGCTGTCCCAATGGGAG-3' (SEQ ID NO: 854)

5'-UGUGAUCCAAGCUGUCCCAAUGGGAGC-3' (SEQ ID NO: 2279)
3'-ACACUAGGUUCGACAGGGUUACCCUCG-5' (SEQ ID NO: 499)

EGFR-840 Target: 5'-TGTGATCCAAGCTGTCCCAATGGGAGC-3' (SEQ ID NO: 855)

5'-GUGAUCCAAGCUGUCCCAAUGGGAGCU-3' (SEQ ID NO: 2280)
3'-CACUAGGUUCGACAGGGUUACCCUCGA-5' (SEQ ID NO: 500)

EGFR-841 Target: 5'-GTGATCCAAGCTGTCCCAATGGGAGCT-3' (SEQ ID NO: 856)

5'-UGAUCCAAGCUGUCCCAAUGGGAGCUG-3' (SEQ ID NO: 2281)
3'-ACUAGGUUCGACAGGGUUACCCUCGAC-5' (SEQ ID NO: 501)

EGFR-842 Target: 5'-TGATCCAAGCTGTCCCAATGGGAGCTG-3' (SEQ ID NO: 857)

5'-GCAGGAGAGGAGAACUGCCAGAAACUG-3' (SEQ ID NO: 2282)
3'-CGUCCUCUCCUCUUGACGGUCUUUGAC-5' (SEQ ID NO: 502)

EGFR-876 Target: 5'-GCAGGAGAGGAGAACTGCCAGAACTG-3' (SEQ ID NO: 858)

5'-CAGGAGAGGAGAACUGCCAGAAACUGA-3' (SEQ ID NO: 2283)

3'-GUCCUCUCCUCUUGACGGUCUUUGACU-5' (SEQ ID NO: 503)

EGFR-877 Target: 5'-CAGGAGAGGAGAACTGCCAGAACTGA-3' (SEQ ID NO: 859)

5'-AGGAGAGGAGAACUGCCAGAAACUGAC-3' (SEQ ID NO: 2284)

3'-UCCUCUCCUCUUGACGGUCUUUGACUG-5' (SEQ ID NO: 504)

EGFR-878 Target: 5'-AGGAGAGGAGAACTGCCAGAACTGAC-3' (SEQ ID NO: 860)

5'-GGAGAGGAGAACUGCCAGAAACUGACC-3' (SEQ ID NO: 2285)

3'-CCUCUCCUCUUGACGGUCUUUGACUGG-5' (SEQ ID NO: 505)

EGFR-879 Target: 5'-GGAGAGGAGAACTGCCAGAACTGACC-3' (SEQ ID NO: 861)

5'-ACUGACCAAAAUCAUCUGUGCCCAGCA-3' (SEQ ID NO: 2286)

3'-UGACUGGUUUUAGUAGACACGGGUCGU-5' (SEQ ID NO: 506)

EGFR-899 Target: 5'-ACTGACCAAAATCATCTGTGCCCAGCA-3' (SEQ ID NO: 862)

5'-CUGACCAAAAUCAUCUGUGCCCAGCAG-3' (SEQ ID NO: 2287)

3'-GACUGGUUUUAGUAGACACGGGUCGUC-5' (SEQ ID NO: 507)

EGFR-900 Target: 5'-CTGACCAAAATCATCTGTGCCCAGCAG-3' (SEQ ID NO: 863)

5'-UGACCAAAAUCAUCUGUGCCCAGCAGU-3' (SEQ ID NO: 2288)

3'-ACUGGUUUUAGUAGACACGGGUCGUCA-5' (SEQ ID NO: 508)

EGFR-901 Target: 5'-TGACCAAAATCATCTGTGCCCAGCAGT-3' (SEQ ID NO: 864)

5'-GACCAAAAUCAUCUGUGCCCAGCAGUG-3' (SEQ ID NO: 2289)

3'-CUGGUUUUAGUAGACACGGGUCGUCAC-5' (SEQ ID NO: 509)

EGFR-902 Target: 5'-GACCAAAATCATCTGTGCCCAGCAGTG-3' (SEQ ID NO: 865)

5'-ACCAAAAUCAUCUGUGCCCAGCAGUGC-3' (SEQ ID NO: 2290)

3'-UGGUUUUAGUAGACACGGGUCGUCACG-5' (SEQ ID NO: 510)

EGFR-903 Target: 5'-ACCAAAATCATCTGTGCCCAGCAGTGC-3' (SEQ ID NO: 866)

5'-CCAAAAUCAUCUGUGCCCAGCAGUGCU-3' (SEQ ID NO: 2291)

3'-GGUUUUAGUAGACACGGGUCGUCACGA-5' (SEQ ID NO: 511)

EGFR-904 Target: 5'-CCAAATCATCTGTGCCCAGCAGTGCT-3' (SEQ ID NO: 867)

5'-CAAAAUCAUCUGUGCCCAGCAGUGCUC-3' (SEQ ID NO: 2292)

3'-GUUUUAGUAGACACGGGUCGUCACGAG-5' (SEQ ID NO: 512)

EGFR-905 Target: 5'-CAAAATCATCTGTGCCCAGCAGTGCTC-3' (SEQ ID NO: 868)

5'-CCCAGUGACUGCUGCCACAACCAGUGU-3' (SEQ ID NO: 2293)

3'-GGGUCACUGACGACGGUGUUGGUCACA-5' (SEQ ID NO: 513)

EGFR-954 Target: 5'-CCCAGTGACTGCTGCCACAACCAGTGT-3' (SEQ ID NO: 869)

5'-CCAGUGACUGCUGCCACAACCAGUGUG-3' (SEQ ID NO: 2294)

3'-GGUCACUGACGACGGUGUUGGUCACAC-5' (SEQ ID NO: 514)

EGFR-955 Target: 5'-CCAGTGACTGCTGCCACAACCAGTGTG-3' (SEQ ID NO: 870)

5'-CAGUGACUGCUGCCACAACCAGUGUGC-3' (SEQ ID NO: 2295)
3'-GUCACUGACGACGGUGUUGGUCACACG-5' (SEQ ID NO: 515)

EGFR-956 Target: 5'-CAGTGACTGCTGCCACAACCAGTGTGC-3' (SEQ ID NO: 871)

5'-CUCACUCUCCAUAAAUGCUACGAAUUAU-3' (SEQ ID NO: 2296)
3'-GAGUGAGAGGUUUUACGAUGCUUAUA-5' (SEQ ID NO: 516)

EGFR-1313 Target: 5'-CTCACTCTCCATAAATGCTACGAATAT-3' (SEQ ID NO: 872)

5'-GGUUUUUGCUGAUUCAGGCUUGGCCUG-3' (SEQ ID NO: 2297)
3'-CCAAAACGACUAAGUCCGAACCGGAC-5' (SEQ ID NO: 517)

EGFR-1480 Target: 5'-GGTTTTTGCTGATTCAGGCTTGGCCTG-3' (SEQ ID NO: 873)

5'-GUUUUUGCUGAUUCAGGCUUGGCCUGA-3' (SEQ ID NO: 2298)
3'-CAAAAACGACUAAGUCCGAACCGGACU-5' (SEQ ID NO: 518)

EGFR-1481 Target: 5'-GTTTTTGCTGATTCAGGCTTGGCCTGA-3' (SEQ ID NO: 874)

5'-UUUUUGCUGAUUCAGGCUUGGCCUGAA-3' (SEQ ID NO: 2299)
3'-AAAAACGACUAAGUCCGAACCGGACUU-5' (SEQ ID NO: 519)

EGFR-1482 Target: 5'-TTTTTGCTGATTCAGGCTTGGCCTGAA-3' (SEQ ID NO: 875)

5'-UUUUGCUGAUUCAGGCUUGGCCUGAAA-3' (SEQ ID NO: 2300)
3'-AAAACGACUAAGUCCGAACCGGACUUU-5' (SEQ ID NO: 520)

EGFR-1483 Target: 5'-TTTTGCTGATTCAGGCTTGGCCTGAAA-3' (SEQ ID NO: 876)

5'-UUUGCUGAUUCAGGCUUGGCCUGAAAA-3' (SEQ ID NO: 2301)
3'-AAACGACUAAGUCCGAACCGGACUUUU-5' (SEQ ID NO: 521)

EGFR-1484 Target: 5'-TTTGCTGATTCAGGCTTGGCCTGAAAA-3' (SEQ ID NO: 877)

5'-UUGCUGAUUCAGGCUUGGCCUGAAAAC-3' (SEQ ID NO: 2302)
3'-AACGACUAAGUCCGAACCGGACUUUUG-5' (SEQ ID NO: 522)

EGFR-1485 Target: 5'-TTGCTGATTCAGGCTTGGCCTGAAAAC-3' (SEQ ID NO: 878)

5'-UGCUGAUUCAGGCUUGGCCUGAAAACA-3' (SEQ ID NO: 2303)
3'-ACGACUAAGUCCGAACCGGACUUUUGU-5' (SEQ ID NO: 523)

EGFR-1486 Target: 5'-TGCTGATTCAGGCTTGGCCTGAAAACA-3' (SEQ ID NO: 879)

5'-GCUGAUUCAGGCUUGGCCUGAAAACAG-3' (SEQ ID NO: 2304)
3'-CGACUAAGUCCGAACCGGACUUUUGUC-5' (SEQ ID NO: 524)

EGFR-1487 Target: 5'-GCTGATTCAGGCTTGGCCTGAAAACAG-3' (SEQ ID NO: 880)

5'-CCAAGCAACAUGGUCAGUUUUUCUCUUG-3' (SEQ ID NO: 2305)
3'-GGUUCGUUGUACCAGUCAAAAGAGAAC-5' (SEQ ID NO: 525)

EGFR-1561 Target: 5'-CCAAGCAACATGGTCAGTTTTCTCTTG-3' (SEQ ID NO: 881)

5'-CAAGCAACAUGGUCAGUUUUUCUCUUGC-3' (SEQ ID NO: 2306)

3'-GUUCGUUGUACCAGUCAAAAAGAGAACG-5' (SEQ ID NO: 526)
EGFR-1562 Target: 5'-CAAGCAACATGGTCAGTTTTCTCTTGCA-3' (SEQ ID NO: 882)

5'-AAGCAACAUGGUCAGUUUUCUCUUGCA-3' (SEQ ID NO: 2307)
3'-UUCGUUGUACCAGUCAAAAAGAGAACGU-5' (SEQ ID NO: 527)
EGFR-1563 Target: 5'-AAGCAACATGGTCAGTTTTCTCTTGCA-3' (SEQ ID NO: 883)

5'-UACAAUAAACUGGAAAAAACUGUUUGG-3' (SEQ ID NO: 2308)
3'-AUGUUAUUUGACCUUUUUUUGACAAACC-5' (SEQ ID NO: 528)
EGFR-1691 Target: 5'-TACAATAAACTGGAAAAAACTGTTTGG-3' (SEQ ID NO: 884)

5'-CUCAGGCCAUGAACAUCAACCUGCACAG-3' (SEQ ID NO: 2309)
3'-GAGUCCGGUACUUGUAGUGGACGUGUC-5' (SEQ ID NO: 529)
EGFR-1963 Target: 5'-CTCAGGCCATGAACATCACCTGCACAG-3' (SEQ ID NO: 885)

5'-UCAGGCCAUGAACAUCAACCUGCACAGG-3' (SEQ ID NO: 2310)
3'-AGUCCGGUACUUGUAGUGGACGUGUCC-5' (SEQ ID NO: 530)
EGFR-1964 Target: 5'-TCAGGCCATGAACATCACCTGCACAGG-3' (SEQ ID NO: 886)

5'-GUAUCCAGUGUGCCCACUACAUUGACG-3' (SEQ ID NO: 2311)
3'-CAUAGGUCACACGGGUGAUGUAAACUGC-5' (SEQ ID NO: 531)
EGFR-2008 Target: 5'-GTATCCAGTGTGCCCCACTACATTGACG-3' (SEQ ID NO: 887)

5'-UAUCCAGUGUGCCCACUACAUUGACGG-3' (SEQ ID NO: 2312)
3'-AUAGGUCACACGGGUGAUGUAAACUGCC-5' (SEQ ID NO: 532)
EGFR-2009 Target: 5'-TATCCAGTGTGCCCCACTACATTGACGG-3' (SEQ ID NO: 888)

5'-AUCCAGUGUGCCCACUACAUUGACGGC-3' (SEQ ID NO: 2313)
3'-UAGGUCACACGGGUGAUGUAAACUGCCG-5' (SEQ ID NO: 533)
EGFR-2010 Target: 5'-ATCCAGTGTGCCCCACTACATTGACGGC-3' (SEQ ID NO: 889)

5'-UCCAGUGUGCCCACUACAUUGACGGCC-3' (SEQ ID NO: 2314)
3'-AGGUCACACGGGUGAUGUAAACUGCCGG-5' (SEQ ID NO: 534)
EGFR-2011 Target: 5'-TCCAGTGTGCCCCACTACATTGACGGCC-3' (SEQ ID NO: 890)

5'-CCAGUGUGCCCACUACAUUGACGGCCC-3' (SEQ ID NO: 2315)
3'-GGUCACACGGGUGAUGUAAACUGCCGGG-5' (SEQ ID NO: 535)
EGFR-2012 Target: 5'-CCAGTGTGCCCCACTACATTGACGGCCC-3' (SEQ ID NO: 891)

5'-CUGAAUUCAAAAAGAUCAAAGUGCUGG-3' (SEQ ID NO: 2316)
3'-GACUUAAGUUUUUCUAGUUUCACGACC-5' (SEQ ID NO: 536)
EGFR-2401 Target: 5'-CTGAATTCAAAAAGATCAAAGTGCTGG-3' (SEQ ID NO: 892)

5'-UGAAUUCAAAAAGAUCAAAGUGCUGGG-3' (SEQ ID NO: 2317)
3'-ACUUAAGUUUUUCUAGUUUCACGACCC-5' (SEQ ID NO: 537)
EGFR-2402 Target: 5'-TGAATTCAAAAAGATCAAAGTGCTGGG-3' (SEQ ID NO: 893)

5'-GACUCUGGAUCCCAGAAGGUGAGAAAAG-3' (SEQ ID NO: 2318)
3'-CUGAGACCUAGGGUCUCCACUCUUUC-5' (SEQ ID NO: 538)
EGFR-2458 Target: 5'-GACTCTGGATCCCAGAAGGTGAGAAAAG-3' (SEQ ID NO: 894)

5'-ACUCUGGAUCCCAGAAGGUGAGAAAAGU-3' (SEQ ID NO: 2319)
3'-UGAGACCUAGGGUCUCCACUCUUUCA-5' (SEQ ID NO: 539)
EGFR-2459 Target: 5'-ACTCTGGATCCCAGAAGGTGAGAAAAGT-3' (SEQ ID NO: 895)

5'-CUCUGGAUCCCAGAAGGUGAGAAAAGUU-3' (SEQ ID NO: 2320)
3'-GAGACCUAGGGUCUCCACUCUUUCA-5' (SEQ ID NO: 540)
EGFR-2460 Target: 5'-CTCTGGATCCCAGAAGGTGAGAAAAGTT-3' (SEQ ID NO: 896)

5'-UCUGGAUCCCAGAAGGUGAGAAAAGUUA-3' (SEQ ID NO: 2321)
3'-AGACCUAGGGUCUCCACUCUUUCAU-5' (SEQ ID NO: 541)
EGFR-2461 Target: 5'-TCTGGATCCCAGAAGGTGAGAAAAGTTA-3' (SEQ ID NO: 897)

5'-CUGGAUCCCAGAAGGUGAGAAAAGUUA-3' (SEQ ID NO: 2322)
3'-GACCUAGGGUCUCCACUCUUUCAU-5' (SEQ ID NO: 542)
EGFR-2462 Target: 5'-CTGGATCCCAGAAGGTGAGAAAAGTTAA-3' (SEQ ID NO: 898)

5'-UGGAUCCCAGAAGGUGAGAAAAGUUA-3' (SEQ ID NO: 2323)
3'-ACCUAGGGUCUCCACUCUUUCAUU-5' (SEQ ID NO: 543)
EGFR-2463 Target: 5'-TGGATCCCAGAAGGTGAGAAAAGTTAAA-3' (SEQ ID NO: 899)

5'-GGAUCCCAGAAGGUGAGAAAAGUUA-3' (SEQ ID NO: 2324)
3'-CCUAGGGUCUCCACUCUUUCAUU-5' (SEQ ID NO: 544)
EGFR-2464 Target: 5'-GGATCCCAGAAGGTGAGAAAAGTTAAAA-3' (SEQ ID NO: 900)

5'-GAUCCCAGAAGGUGAGAAAAGUUA-3' (SEQ ID NO: 2325)
3'-CUAGGGUCUCCACUCUUUCAUU-5' (SEQ ID NO: 545)
EGFR-2465 Target: 5'-GATCCCAGAAGGTGAGAAAAGTTAAAAT-3' (SEQ ID NO: 901)

5'-CGCAGCAUGUCAAGAUCACAGAUUUUG-3' (SEQ ID NO: 2326)
3'-GCGUCGUACAGUUCUAGUGUCUAAAAC-5' (SEQ ID NO: 546)
EGFR-2815 Target: 5'-CGCAGCATGTCAAGATCACAGATTTTG-3' (SEQ ID NO: 902)

5'-GCAGCAUGUCAAGAUCACAGAUUUUGG-3' (SEQ ID NO: 2327)
3'-CGUCGUACAGUUCUAGUGUCUAAAACC-5' (SEQ ID NO: 547)
EGFR-2816 Target: 5'-GCAGCATGTCAAGATCACAGATTTTGG-3' (SEQ ID NO: 903)

5'-CAGCAUGUCAAGAUCACAGAUUUUGGG-3' (SEQ ID NO: 2328)
3'-GUCGUACAGUUCUAGUGUCUAAAACCC-5' (SEQ ID NO: 548)
EGFR-2817 Target: 5'-CAGCATGTCAAGATCACAGATTTTGGG-3' (SEQ ID NO: 904)

5'-AGCAUGUCAAGAUCACAGAUUUUGGGC-3' (SEQ ID NO: 2329)
3'-UCGUACAGUUCUAGUGUCUAAAACCCG-5' (SEQ ID NO: 549)
EGFR-2818 Target: 5'-AGCATGTCAAGATCACAGATTTTGGGC-3' (SEQ ID NO: 905)

5'-GCAUGUCAAGAUCACAGAUUUUGGGCU-3' (SEQ ID NO: 2330)
3'-CGUACAGUUCUAGUGUCUAAAACCCGA-5' (SEQ ID NO: 550)
EGFR-2819 Target: 5'-GCATGTCAAGATCACAGATTTTGGGCT-3' (SEQ ID NO: 906)

5'-CAUGUCAAGAUCACAGAUUUUGGGCUG-3' (SEQ ID NO: 2331)
3'-GUACAGUUCUAGUGUCUAAAACCCGAC-5' (SEQ ID NO: 551)
EGFR-2820 Target: 5'-CATGTCAAGATCACAGATTTTGGGCTG-3' (SEQ ID NO: 907)

5'-AUGUCAAGAUCACAGAUUUUGGGCUGG-3' (SEQ ID NO: 2332)
3'-UACAGUUCUAGUGUCUAAAACCCGACC-5' (SEQ ID NO: 552)
EGFR-2821 Target: 5'-ATGTCAAGATCACAGATTTTGGGCTGG-3' (SEQ ID NO: 908)

5'-UGUCAAGAUCACAGAUUUUGGGCUGGC-3' (SEQ ID NO: 2333)
3'-ACAGUUCUAGUGUCUAAAACCCGACCG-5' (SEQ ID NO: 553)
EGFR-2822 Target: 5'-TGTCAAGATCACAGATTTTGGGCTGGC-3' (SEQ ID NO: 909)

5'-GUCAAGAUCACAGAUUUUGGGCUGGCC-3' (SEQ ID NO: 2334)
3'-CAGUUCUAGUGUCUAAAACCCGACCGG-5' (SEQ ID NO: 554)
EGFR-2823 Target: 5'-GTCAAGATCACAGATTTTGGGCTGGCC-3' (SEQ ID NO: 910)

5'-UCAAGAUCACAGAUUUUGGGCUGGCCA-3' (SEQ ID NO: 2335)
3'-AGUUCUAGUGUCUAAAACCCGACCGGU-5' (SEQ ID NO: 555)
EGFR-2824 Target: 5'-TCAAGATCACAGATTTTGGGCTGGCCA-3' (SEQ ID NO: 911)

5'-CAAGAUCACAGAUUUUGGGCUGGCCAA-3' (SEQ ID NO: 2336)
3'-GUUCUAGUGUCUAAAACCCGACCGGUU-5' (SEQ ID NO: 556)
EGFR-2825 Target: 5'-CAAGATCACAGATTTTGGGCTGGCCAA-3' (SEQ ID NO: 912)

5'-AAGAUCACAGAUUUUGGGCUGGCCAAA-3' (SEQ ID NO: 2337)
3'-UUCUAGUGUCUAAAACCCGACCGGUUU-5' (SEQ ID NO: 557)
EGFR-2826 Target: 5'-AAGATCACAGATTTTGGGCTGGCCAAA-3' (SEQ ID NO: 913)

5'-AGAUCACAGAUUUUGGGCUGGCCAAAC-3' (SEQ ID NO: 2338)
3'-UCUAGUGUCUAAAACCCGACCGGUUUG-5' (SEQ ID NO: 558)
EGFR-2827 Target: 5'-AGATCACAGATTTTGGGCTGGCCAAAC-3' (SEQ ID NO: 914)

5'-GAUCACAGAUUUUGGGCUGGCCAAACU-3' (SEQ ID NO: 2339)
3'-CUAGUGUCUAAAACCCGACCGGUUUGA-5' (SEQ ID NO: 559)
EGFR-2828 Target: 5'-GATCACAGATTTTGGGCTGGCCAAACT-3' (SEQ ID NO: 915)

5'-AUCACAGAUUUUGGGCUGGCCAAACUG-3' (SEQ ID NO: 2340)
3'-UAGUGUCUAAAACCCGACCGGUUUGAC-5' (SEQ ID NO: 560)
EGFR-2829 Target: 5'-ATCACAGATTTTGGGCTGGCCAAACTG-3' (SEQ ID NO: 916)

5'-UCACAGAUUUUGGGCUGGCCAAACUGC-3' (SEQ ID NO: 2341)
3'-AGUGUCUAAAACCCGACCGGUUUGACG-5' (SEQ ID NO: 561)

EGFR-2830 Target: 5'-TCACAGATTTTGGGCTGGCCAAACTGC-3' (SEQ ID NO: 917)

5'-CACAGAUUUUGGGCUGGCCAAACUGCU-3' (SEQ ID NO: 2342)

3'-GUGUCUAAAACCCGACCGGUUUGACGA-5' (SEQ ID NO: 562)

EGFR-2831 Target: 5'-CACAGATTTTGGGCTGGCCAAACTGCT-3' (SEQ ID NO: 918)

5'-ACAGAUUUUGGGCUGGCCAAACUGCUG-3' (SEQ ID NO: 2343)

3'-UGUCUAAAACCCGACCGGUUUGACGAC-5' (SEQ ID NO: 563)

EGFR-2832 Target: 5'-ACAGATTTTGGGCTGGCCAAACTGCTG-3' (SEQ ID NO: 919)

5'-CAGAUUUUGGGCUGGCCAAACUGCUGG-3' (SEQ ID NO: 2344)

3'-GUCUAAAACCCGACCGGUUUGACGACC-5' (SEQ ID NO: 564)

EGFR-2833 Target: 5'-CAGATTTTGGGCTGGCCAAACTGCTGG-3' (SEQ ID NO: 920)

5'-AGAUUUUGGGCUGGCCAAACUGCUGGG-3' (SEQ ID NO: 2345)

3'-UCUAAAACCCGACCGGUUUGACGACCC-5' (SEQ ID NO: 565)

EGFR-2834 Target: 5'-AGATTTTGGGCTGGCCAAACTGCTGGG-3' (SEQ ID NO: 921)

5'-GAUUUUGGGCUGGCCAAACUGCUGGGU-3' (SEQ ID NO: 2346)

3'-CUAAAACCCGACCGGUUUGACGACCCA-5' (SEQ ID NO: 566)

EGFR-2835 Target: 5'-GATTTTGGGCTGGCCAAACTGCTGGGT-3' (SEQ ID NO: 922)

5'-AUUUUGGGCUGGCCAAACUGCUGGGUG-3' (SEQ ID NO: 2347)

3'-UAAAACCCGACCGGUUUGACGACCCAC-5' (SEQ ID NO: 567)

EGFR-2836 Target: 5'-ATTTTGGGCTGGCCAAACTGCTGGGTG-3' (SEQ ID NO: 923)

5'-UUUUGGGCUGGCCAAACUGCUGGGUGC-3' (SEQ ID NO: 2348)

3'-AAAACCCGACCGGUUUGACGACCCACG-5' (SEQ ID NO: 568)

EGFR-2837 Target: 5'-TTTTGGGCTGGCCAAACTGCTGGGTGC-3' (SEQ ID NO: 924)

5'-AGGCAAAGUGCCUAUCAAGUGGAUGGC-3' (SEQ ID NO: 2349)

3'-UCCGUUUCACGGAUAGUUCACCUACCG-5' (SEQ ID NO: 569)

EGFR-2891 Target: 5'-AGGCAAAGTGCCTATCAAGTGGATGGC-3' (SEQ ID NO: 925)

5'-GGCAAAGUGCCUAUCAAGUGGAUGGCA-3' (SEQ ID NO: 2350)

3'-CCGUUUCACGGAUAGUUCACCUACCGU-5' (SEQ ID NO: 570)

EGFR-2892 Target: 5'-GGCAAAGTGCCTATCAAGTGGATGGCA-3' (SEQ ID NO: 926)

5'-GCAAAGUGCCUAUCAAGUGGAUGGCAU-3' (SEQ ID NO: 2351)

3'-CGUUUCACGGAUAGUUCACCUACCGUA-5' (SEQ ID NO: 571)

EGFR-2893 Target: 5'-GCAAAGTGCCTATCAAGTGGATGGCAT-3' (SEQ ID NO: 927)

5'-CAAAGUGCCUAUCAAGUGGAUGGCAUU-3' (SEQ ID NO: 2352)

3'-GUUUCACGGAUAGUUCACCUACCGUAA-5' (SEQ ID NO: 572)

EGFR-2894 Target: 5'-CAAAGTGCCTATCAAGTGGATGGCATT-3' (SEQ ID NO: 928)

5'-AAAGUGCCUAUCAAGUGGAUGGCAUUG-3' (SEQ ID NO: 2353)

3'-UUUCACGGAUAGUUCACCUACCGUAAC-5' (SEQ ID NO: 573)
EGFR-2895 Target: 5'-AAAGTGCCTATCAAGTGGATGGCATTG-3' (SEQ ID NO: 929)

5'-AAGUGCCUAUCAAGUGGAUGGCAUUGG-3' (SEQ ID NO: 2354)
3'-UUCACGGAUAGUUCACCUACCGUAACC-5' (SEQ ID NO: 574)
EGFR-2896 Target: 5'-AAGTGCCTATCAAGTGGATGGCATTGG-3' (SEQ ID NO: 930)

5'-AGUGCCUAUCAAGUGGAUGGCAUUGGA-3' (SEQ ID NO: 2355)
3'-UCACGGAUAGUUCACCUACCGUAACCU-5' (SEQ ID NO: 575)
EGFR-2897 Target: 5'-AGTGCCTATCAAGTGGATGGCATTGGA-3' (SEQ ID NO: 931)

5'-GUACCAUCGAUGUCUACAUGAUGG-3' (SEQ ID NO: 2356)
3'-CAUGGUAGCUACAGAUGUACUAGUACC-5' (SEQ ID NO: 576)
EGFR-3088 Target: 5'-GTACCATCGATGTCTACATGATCATGG-3' (SEQ ID NO: 932)

5'-UACCAUCGAUGUCUACAUGAUGGU-3' (SEQ ID NO: 2357)
3'-AUGGUAGCUACAGAUGUACUAGUACCA-5' (SEQ ID NO: 577)
EGFR-3089 Target: 5'-TACCATCGATGTCTACATGATCATGGT-3' (SEQ ID NO: 933)

5'-ACCAUCGAUGUCUACAUGAUGGUC-3' (SEQ ID NO: 2358)
3'-UGGUAGCUACAGAUGUACUAGUACCAG-5' (SEQ ID NO: 578)
EGFR-3090 Target: 5'-ACCATCGATGTCTACATGATCATGGTC-3' (SEQ ID NO: 934)

5'-CCAUCGAUGUCUACAUGAUGGUCA-3' (SEQ ID NO: 2359)
3'-GGUAGCUACAGAUGUACUAGUACCAGU-5' (SEQ ID NO: 579)
EGFR-3091 Target: 5'-CCATCGATGTCTACATGATCATGGTCA-3' (SEQ ID NO: 935)

5'-CAUCGAUGUCUACAUGAUGGUCAA-3' (SEQ ID NO: 2360)
3'-GUAGCUACAGAUGUACUAGUACCAGUU-5' (SEQ ID NO: 580)
EGFR-3092 Target: 5'-CATCGATGTCTACATGATCATGGTCAA-3' (SEQ ID NO: 936)

5'-AUCGAUGUCUACAUGAUGGUCAAG-3' (SEQ ID NO: 2361)
3'-UAGCUACAGAUGUACUAGUACCAGUUC-5' (SEQ ID NO: 581)
EGFR-3093 Target: 5'-ATCGATGTCTACATGATCATGGTCAAG-3' (SEQ ID NO: 937)

5'-UCGAUGUCUACAUGAUGGUCAAGU-3' (SEQ ID NO: 2362)
3'-AGCUACAGAUGUACUAGUACCAGUUCA-5' (SEQ ID NO: 582)
EGFR-3094 Target: 5'-TCGATGTCTACATGATCATGGTCAAGT-3' (SEQ ID NO: 938)

5'-CGAUGUCUACAUGAUGGUCAAGUG-3' (SEQ ID NO: 2363)
3'-GCUACAGAUGUACUAGUACCAGUUCAC-5' (SEQ ID NO: 583)
EGFR-3095 Target: 5'-CGATGTCTACATGATCATGGTCAAGTG-3' (SEQ ID NO: 939)

5'-GAUGUCUACAUGAUGGUCAAGUGC-3' (SEQ ID NO: 2364)
3'-CUACAGAUGUACUAGUACCAGUUCACG-5' (SEQ ID NO: 584)
EGFR-3096 Target: 5'-GATGTCTACATGATCATGGTCAAGTGC-3' (SEQ ID NO: 940)

5'-AUGUCUACAUGAUGAUGGUCAAGUGCU-3' (SEQ ID NO: 2365)
3'-UACAGAUAGUACUAGUACCAGUUCACGA-5' (SEQ ID NO: 585)
EGFR-3097 Target: 5'-ATGTCTACATGATCATGGTCAAGTGCT-3' (SEQ ID NO: 941)

5'-UGUCUACAUGAUGAUGGUCAAGUGCUG-3' (SEQ ID NO: 2366)
3'-ACAGAUAGUACUAGUACCAGUUCACGAC-5' (SEQ ID NO: 586)
EGFR-3098 Target: 5'-TGTCTACATGATCATGGTCAAGTGCTG-3' (SEQ ID NO: 942)

5'-GUCUACAUGAUGAUGGUCAAGUGCUGG-3' (SEQ ID NO: 2367)
3'-CAGAUAGUACUAGUACCAGUUCACGACC-5' (SEQ ID NO: 587)
EGFR-3099 Target: 5'-GTCTACATGATCATGGTCAAGTGCTGG-3' (SEQ ID NO: 943)

5'-UCUACAUGAUGAUGGUCAAGUGCUGGA-3' (SEQ ID NO: 2368)
3'-AGAUGUACUAGUACCAGUUCACGACCU-5' (SEQ ID NO: 588)
EGFR-3100 Target: 5'-TCTACATGATCATGGTCAAGTGCTGGA-3' (SEQ ID NO: 944)

5'-CUACAUGAUGAUGGUCAAGUGCUGGAU-3' (SEQ ID NO: 2369)
3'-GAUGUACUAGUACCAGUUCACGACCUA-5' (SEQ ID NO: 589)
EGFR-3101 Target: 5'-CTACATGATCATGGTCAAGTGCTGGAT-3' (SEQ ID NO: 945)

5'-UACAUGAUGAUGGUCAAGUGCUGGAUG-3' (SEQ ID NO: 2370)
3'-AUGUACUAGUACCAGUUCACGACCUAC-5' (SEQ ID NO: 590)
EGFR-3102 Target: 5'-TACATGATCATGGTCAAGTGCTGGATG-3' (SEQ ID NO: 946)

5'-ACAUGAUGAUGGUCAAGUGCUGGAUGA-3' (SEQ ID NO: 2371)
3'-UGUACUAGUACCAGUUCACGACCUACU-5' (SEQ ID NO: 591)
EGFR-3103 Target: 5'-ACATGATCATGGTCAAGTGCTGGATGA-3' (SEQ ID NO: 947)

5'-CAUGAUGAUGGUCAAGUGCUGGAUGAU-3' (SEQ ID NO: 2372)
3'-GUACUAGUACCAGUUCACGACCUACUA-5' (SEQ ID NO: 592)
EGFR-3104 Target: 5'-CATGATCATGGTCAAGTGCTGGATGAT-3' (SEQ ID NO: 948)

5'-AUGAUGAUGGUCAAGUGCUGGAUGAUA-3' (SEQ ID NO: 2373)
3'-UACUAGUACCAGUUCACGACCUACUAU-5' (SEQ ID NO: 593)
EGFR-3105 Target: 5'-ATGATCATGGTCAAGTGCTGGATGATA-3' (SEQ ID NO: 949)

5'-UGAUGAUGGUCAAGUGCUGGAUGAUAG-3' (SEQ ID NO: 2374)
3'-ACUAGUACCAGUUCACGACCUACUAUC-5' (SEQ ID NO: 594)
EGFR-3106 Target: 5'-TGATCATGGTCAAGTGCTGGATGATAG-3' (SEQ ID NO: 950)

5'-GAUGAUGGUCAAGUGCUGGAUGAUAGA-3' (SEQ ID NO: 2375)
3'-CUAGUACCAGUUCACGACCUACUAUCU-5' (SEQ ID NO: 595)
EGFR-3107 Target: 5'-GATCATGGTCAAGTGCTGGATGATAGA-3' (SEQ ID NO: 951)

5'-AUCAUGGUCAAGUGCUGGAUGAUAGAC-3' (SEQ ID NO: 2376)
3'-UAGUACCAGUUCACGACCUACUAUCUG-5' (SEQ ID NO: 596)
EGFR-3108 Target: 5'-ATCATGGTCAAGTGCTGGATGATAGAC-3' (SEQ ID NO: 952)

5'-UCAUGGUCAAGUGCUGGAUGAUAGACG-3' (SEQ ID NO: 2377)
3'-AGUACCAGUUCACGACCUACUAUCUGC-5' (SEQ ID NO: 597)
EGFR-3109 Target: 5'-TCATGGTCAAGTGCTGGATGATAGACG-3' (SEQ ID NO: 953)

5'-CAUGGUCAAGUGCUGGAUGAUAGACGC-3' (SEQ ID NO: 2378)
3'-GUACCAGUUCACGACCUACUAUCUGCG-5' (SEQ ID NO: 598)
EGFR-3110 Target: 5'-CATGGTCAAGTGCTGGATGATAGACGC-3' (SEQ ID NO: 954)

5'-AUGGUCAAGUGCUGGAUGAUAGACGCA-3' (SEQ ID NO: 2379)
3'-UACCAGUUCACGACCUACUAUCUGCGU-5' (SEQ ID NO: 599)
EGFR-3111 Target: 5'-ATGGTCAAGTGCTGGATGATAGACGCA-3' (SEQ ID NO: 955)

5'-UGGUCAAGUGCUGGAUGAUAGACGCAG-3' (SEQ ID NO: 2380)
3'-ACCAGUUCACGACCUACUAUCUGCGUC-5' (SEQ ID NO: 600)
EGFR-3112 Target: 5'-TGGTCAAGTGCTGGATGATAGACGCAG-3' (SEQ ID NO: 956)

5'-GGUCAAGUGCUGGAUGAUAGACGCAGA-3' (SEQ ID NO: 2381)
3'-CCAGUUCACGACCUACUAUCUGCGUCU-5' (SEQ ID NO: 601)
EGFR-3113 Target: 5'-GGTCAAGTGCTGGATGATAGACGCAGA-3' (SEQ ID NO: 957)

5'-UCGAAUUCUCCAAAAUGGCCCCGAGACC-3' (SEQ ID NO: 2382)
3'-AGCUUAAGAGGUUUUACCGGGCUCUGG-5' (SEQ ID NO: 602)
EGFR-3169 Target: 5'-TCGAATTCTCCAAAATGGCCCCGAGACC-3' (SEQ ID NO: 958)

5'-CGAAUUCUCCAAAAUGGCCCCGAGACCC-3' (SEQ ID NO: 2383)
3'-GCUUAAGAGGUUUUACCGGGCUCUGGG-5' (SEQ ID NO: 603)
EGFR-3170 Target: 5'-CGAATTCTCCAAAATGGCCCCGAGACCC-3' (SEQ ID NO: 959)

5'-GGGAUGAAAGAAUGCAUUUGCCAAGUC-3' (SEQ ID NO: 2384)
3'-CCCUACUUUCUUACGUAAACGGUUCAG-5' (SEQ ID NO: 604)
EGFR-3220 Target: 5'-GGGATGAAAGAATGCATTTGCCAAGTC-3' (SEQ ID NO: 960)

5'-GGAUGAAAGAAUGCAUUUGCCAAGUCC-3' (SEQ ID NO: 2385)
3'-CCUACUUUCUUACGUAAACGGUUCAGG-5' (SEQ ID NO: 605)
EGFR-3221 Target: 5'-GGATGAAAGAATGCATTTGCCAAGTCC-3' (SEQ ID NO: 961)

5'-GAUGAAAGAAUGCAUUUGCCAAGUCCU-3' (SEQ ID NO: 2386)
3'-CUACUUUCUUACGUAAACGGUUCAGGA-5' (SEQ ID NO: 606)
EGFR-3222 Target: 5'-GATGAAAGAATGCATTTGCCAAGTCCT-3' (SEQ ID NO: 962)

5'-AUGAAAGAAUGCAUUUGCCAAGUCCUA-3' (SEQ ID NO: 2387)
3'-UACUUUCUUACGUAAACGGUUCAGGAU-5' (SEQ ID NO: 607)
EGFR-3223 Target: 5'-ATGAAAGAATGCATTTGCCAAGTCCTA-3' (SEQ ID NO: 963)

5'-UGAAAGAAUGCAUUUGCCAAGUCCUAC-3' (SEQ ID NO: 2388)
3'-ACUUUCUUACGUAAACGGUUCAGGAUG-5' (SEQ ID NO: 608)

EGFR-3224 Target: 5'-TGAAAGAATGCATTTGCCAAGTCCTAC-3' (SEQ ID NO: 964)

5'-UGGACAACCCUGACUACCAGCAGGACU-3' (SEQ ID NO: 2389)

3'-ACCUGUUGGGACUGAUGGUCGUCCUGA-5' (SEQ ID NO: 609)

EGFR-3772 Target: 5'-TGGACAACCCTGACTACCAGCAGGACT-3' (SEQ ID NO: 965)

5'-GGACAACCCUGACUACCAGCAGGACUU-3' (SEQ ID NO: 2390)

3'-CCUGUUGGGACUGAUGGUCGUCCUGAA-5' (SEQ ID NO: 610)

EGFR-3773 Target: 5'-GGACAACCCTGACTACCAGCAGGACTT-3' (SEQ ID NO: 966)

5'-GACAACCCUGACUACCAGCAGGACUUC-3' (SEQ ID NO: 2391)

3'-CUGUUGGGACUGAUGGUCGUCCUGAAG-5' (SEQ ID NO: 611)

EGFR-3774 Target: 5'-GACAACCCTGACTACCAGCAGGACTTC-3' (SEQ ID NO: 967)

5'-ACAACCCUGACUACCAGCAGGACUUCU-3' (SEQ ID NO: 2392)

3'-UGUUGGGACUGAUGGUCGUCCUGAAGA-5' (SEQ ID NO: 612)

EGFR-3775 Target: 5'-ACAACCCTGACTACCAGCAGGACTTCT-3' (SEQ ID NO: 968)

5'-CAACCCUGACUACCAGCAGGACUUCUU-3' (SEQ ID NO: 2393)

3'-GUUGGGACUGAUGGUCGUCCUGAAGAA-5' (SEQ ID NO: 613)

EGFR-3776 Target: 5'-CAACCCTGACTACCAGCAGGACTTCTT-3' (SEQ ID NO: 969)

5'-AACCCUGACUACCAGCAGGACUUCUUU-3' (SEQ ID NO: 2394)

3'-UUGGGACUGAUGGUCGUCCUGAAGAAA-5' (SEQ ID NO: 614)

EGFR-3777 Target: 5'-AACCCCTGACTACCAGCAGGACTTCTTT-3' (SEQ ID NO: 970)

5'-ACCCUGACUACCAGCAGGACUUCUUUC-3' (SEQ ID NO: 2395)

3'-UGGGACUGAUGGUCGUCCUGAAGAAAAG-5' (SEQ ID NO: 615)

EGFR-3778 Target: 5'-ACCCTGACTACCAGCAGGACTTCTTTC-3' (SEQ ID NO: 971)

5'-CCCUGACUACCAGCAGGACUUCUUUCC-3' (SEQ ID NO: 2396)

3'-GGGACUGAUGGUCGUCCUGAAGAAAAGG-5' (SEQ ID NO: 616)

EGFR-3779 Target: 5'-CCCTGACTACCAGCAGGACTTCTTTCC-3' (SEQ ID NO: 972)

Table 10: Selected Mouse Anti-EGFR "Blunt/Blunt" DsiRNAs

5'-CAGCGCAACGCGCAGCAGCCUCCCUCC-3' (SEQ ID NO: 2397)

3'-GUCGCGUUGCGCGUCGUCGGAGGGAGG-5' (SEQ ID NO: 617)

EGFR-m71 Target: 5'-CAGCGCAACGCGCAGCAGCCTCCCTCC-3' (SEQ ID NO: 973)

5'-ACGCGCAGCAGCCUCCCUCCUCUUCUU-3' (SEQ ID NO: 2398)

3'-UGCGCGUCGUCGGAGGGAGGAGAAGAA-5' (SEQ ID NO: 618)

EGFR-m78 Target: 5'-ACGCGCAGCAGCCTCCCTCCTTCTT-3' (SEQ ID NO: 974)

5'-AGCCUCCCUCCUCUUCUUCUCCCGCACUG-3' (SEQ ID NO: 2399)

3'-UCGGAGGGAGGAGAAGAAGGGCGUGAC-5' (SEQ ID NO: 619)

EGFR-m87 Target: 5'-AGCCTCCCTCCTTCTTCTTCCCGCACTG-3' (SEQ ID NO: 975)

5'-CUCCCCUCCUCUUCUCCCCGCACUGUGC-3' (SEQ ID NO: 2400)
3'-GAGGGAGGAGAAGAAGGGCGUGACACG-5' (SEQ ID NO: 620)
EGFR-m90 Target: 5'-CTCCCTCCTCTTCTTCCCGCACTGTGC-3' (SEQ ID NO: 976)

5'-CCCUCUCCUCUUCUCCCCGCACUGUGCGC-3' (SEQ ID NO: 2401)
3'-GGGAGGAGAAGAAGGGCGUGACACGCG-5' (SEQ ID NO: 621)
EGFR-m92 Target: 5'-CCCTCCTCTTCTTCCCGCACTGTGCGC-3' (SEQ ID NO: 977)

5'-CUCCUCUUCUUCUCCCCGCACUGUGCGCUC-3' (SEQ ID NO: 2402)
3'-GAGGAGAAGAAGGGCGUGACACGCGAG-5' (SEQ ID NO: 622)
EGFR-m94 Target: 5'-CTCCTCTTCTTCCCGCACTGTGCGCTC-3' (SEQ ID NO: 978)

5'-CUCUUCUUCUCCCCGCACUGUGCGCUCCUC-3' (SEQ ID NO: 2403)
3'-GAGAAGAAGGGCGUGACACGCGAGGAG-5' (SEQ ID NO: 623)
EGFR-m97 Target: 5'-CTCTTCTTCCCGCACTGTGCGCTCCTC-3' (SEQ ID NO: 979)

5'-CUUCUUCUCCCCGCACUGUGCGCUCCUCCU-3' (SEQ ID NO: 2404)
3'-GAAGAAGGGCGUGACACGCGAGGAGGA-5' (SEQ ID NO: 624)
EGFR-m99 Target: 5'-CTTCTTCCCGCACTGTGCGCTCCTCCT-3' (SEQ ID NO: 980)

5'-UUCUUCUCCCCGCACUGUGCGCUCCUCCUG-3' (SEQ ID NO: 2405)
3'-AAGAAGGGCGUGACACGCGAGGAGGAC-5' (SEQ ID NO: 625)
EGFR-m100 Target: 5'-TTCTTCCCGCACTGTGCGCTCCTCCTG-3' (SEQ ID NO: 981)

5'-UCUUCUCCCCGCACUGUGCGCUCCUCCUGG-3' (SEQ ID NO: 2406)
3'-AGAAGGGCGUGACACGCGAGGAGGACC-5' (SEQ ID NO: 626)
EGFR-m101 Target: 5'-TCTTCCCGCACTGTGCGCTCCTCCTGG-3' (SEQ ID NO: 982)

5'-CUGUGCGCUCCUCCUGGGCUAGGGCGU-3' (SEQ ID NO: 2407)
3'-GACACGCGAGGAGGACCCGAUCCCGCA-5' (SEQ ID NO: 627)
EGFR-m111 Target: 5'-CTGTGCGCTCCTCCTGGGCTAGGGCGT-3' (SEQ ID NO: 983)

5'-UGCGCUCCUCCUGGGCUAGGGCGUCUG-3' (SEQ ID NO: 2408)
3'-ACGCGAGGAGGACCCGAUCCCGCAGAC-5' (SEQ ID NO: 628)
EGFR-m114 Target: 5'-TGCGCTCCTCCTGGGCTAGGGCGTCTG-3' (SEQ ID NO: 984)

5'-CACACUGCUGGUGUUGCUGACCGCGCU-3' (SEQ ID NO: 2409)
3'-GUGUGACGACCACAACGACUGGCGCGA-5' (SEQ ID NO: 629)
EGFR-m333 Target: 5'-CACACTGCTGGTGTGCTGACCGCGCT-3' (SEQ ID NO: 985)

5'-ACACUGCUGGUGUUGCUGACCGCGCUC-3' (SEQ ID NO: 2410)
3'-UGUGACGACCACAACGACUGGCGCGAG-5' (SEQ ID NO: 630)
EGFR-m334 Target: 5'-ACACTGCTGGTGTGCTGACCGCGCTC-3' (SEQ ID NO: 986)

5'-CACUGCUGGUGUUGCUGACCGCGCUCU-3' (SEQ ID NO: 2411)
3'-GUGACGACCACAACGACUGGCGCGAGA-5' (SEQ ID NO: 631)

EGFR-m335 Target: 5'-CACTGCTGGTGTGCTGACCGCGCTCT-3' (SEQ ID NO: 987)

5'-ACUGCUGGUGUUGCUGACCGCGCUCUG-3' (SEQ ID NO: 2412)

3'-UGACGACCACAACGACUGGCGCGAGAC-5' (SEQ ID NO: 632)

EGFR-m336 Target: 5'-ACTGCTGGTGTGCTGACCGCGCTCTG-3' (SEQ ID NO: 988)

5'-CUGCUGGUGUUGCUGACCGCGCUCUGC-3' (SEQ ID NO: 2413)

3'-GACGACCACAACGACUGGCGCGAGACG-5' (SEQ ID NO: 633)

EGFR-m337 Target: 5'-CTGCTGGTGTGCTGACCGCGCTCTGC-3' (SEQ ID NO: 989)

5'-UGCUGGUGUUGCUGACCGCGCUCUGCG-3' (SEQ ID NO: 2414)

3'-ACGACCACAACGACUGGCGCGAGACGC-5' (SEQ ID NO: 634)

EGFR-m338 Target: 5'-TGCTGGTGTGCTGACCGCGCTCTGCG-3' (SEQ ID NO: 990)

5'-GCUGGUGUUGCUGACCGCGCUCUGCGC-3' (SEQ ID NO: 2415)

3'-CGACCACAACGACUGGCGCGAGACGCG-5' (SEQ ID NO: 635)

EGFR-m339 Target: 5'-GCTGGTGTGCTGACCGCGCTCTGCGC-3' (SEQ ID NO: 991)

5'-UGGUGUUGCUGACCGCGCUCUGCGCCG-3' (SEQ ID NO: 2416)

3'-ACCACAACGACUGGCGCGAGACGCGGC-5' (SEQ ID NO: 636)

EGFR-m341 Target: 5'-TGGTGTGCTGACCGCGCTCTGCGCCG-3' (SEQ ID NO: 992)

5'-GGUGUUGCUGACCGCGCUCUGCGCCGC-3' (SEQ ID NO: 2417)

3'-CCACAACGACUGGCGCGAGACGCGGCG-5' (SEQ ID NO: 637)

EGFR-m342 Target: 5'-GGTGTGCTGACCGCGCTCTGCGCCGC-3' (SEQ ID NO: 993)

5'-GUGUUGCUGACCGCGCUCUGCGCCGCA-3' (SEQ ID NO: 2418)

3'-CACAACGACUGGCGCGAGACGCGGCGU-5' (SEQ ID NO: 638)

EGFR-m343 Target: 5'-GTGTTGCTGACCGCGCTCTGCGCCGCA-3' (SEQ ID NO: 994)

5'-UGUUGCUGACCGCGCUCUGCGCCGCAG-3' (SEQ ID NO: 2419)

3'-ACAACGACUGGCGCGAGACGCGGCGUC-5' (SEQ ID NO: 639)

EGFR-m344 Target: 5'-TGTTGCTGACCGCGCTCTGCGCCGCAG-3' (SEQ ID NO: 995)

5'-UGCUGACCGCGCUCUGCGCCGCAGGUG-3' (SEQ ID NO: 2420)

3'-ACGACUGGCGCGAGACGCGGCGUCCAC-5' (SEQ ID NO: 640)

EGFR-m347 Target: 5'-TGCTGACCGCGCTCTGCGCCGCAGGTG-3' (SEQ ID NO: 996)

5'-GCUGACCGCGCUCUGCGCCGCAGGUGG-3' (SEQ ID NO: 2421)

3'-CGACUGGCGCGAGACGCGGCGUCCACC-5' (SEQ ID NO: 641)

EGFR-m348 Target: 5'-GCTGACCGCGCTCTGCGCCGCAGGTGG-3' (SEQ ID NO: 997)

5'-UCCUGAUUGGUGCUGUGCGAUUCAGCA-3' (SEQ ID NO: 2422)

3'-AGGACUAACCACGACACGCUAAGUCGU-5' (SEQ ID NO: 642)

EGFR-m734 Target: 5'-TCCTGATTGGTGCTGTGCGATTGAGCA-3' (SEQ ID NO: 998)

5'-CCUGAUUGGUGCUGUGCGAUUCAGCAA-3' (SEQ ID NO: 2423)

3'-GGACUAACCACGACACGCUAAGUCGUU-5' (SEQ ID NO: 643)
EGFR-m735 Target: 5'-CCTGATTGGTGCTGTGCGATTCAAGCAA-3' (SEQ ID NO: 999)

5'-CUGAUUGGUGCUGUGCGAUUCAGCAAC-3' (SEQ ID NO: 2424)
3'-GACUAACCACGACACGCUAAGUCGUUG-5' (SEQ ID NO: 644)
EGFR-m736 Target: 5'-CTGATTGGTGCTGTGCGATTCAAGCAA-3' (SEQ ID NO: 1000)

5'-GAUUGGUGCUGUGCGAUUCAGCAACAA-3' (SEQ ID NO: 2425)
3'-CUAACCACGACACGCUAAGUCGUUGUU-5' (SEQ ID NO: 645)
EGFR-m738 Target: 5'-GATTGGTGCTGTGCGATTCAAGCAA-3' (SEQ ID NO: 1001)

5'-UUGGUGCUGUGCGAUUCAGCAACAACC-3' (SEQ ID NO: 2426)
3'-AACCACGACACGCUAAGUCGUUGUUGG-5' (SEQ ID NO: 646)
EGFR-m740 Target: 5'-TTGGTGCTGTGCGATTCAAGCAAACC-3' (SEQ ID NO: 1002)

5'-UGGUGCUGUGCGAUUCAGCAACAACCC-3' (SEQ ID NO: 2427)
3'-ACCACGACACGCUAAGUCGUUGUUGGG-5' (SEQ ID NO: 647)
EGFR-m741 Target: 5'-TGGTGCTGTGCGATTCAAGCAAACCC-3' (SEQ ID NO: 1003)

5'-UCCAAGCUGUCCCAAUGGAAGCUGCUG-3' (SEQ ID NO: 2428)
3'-AGGUUCGACAGGGUUACCUUCGACGAC-5' (SEQ ID NO: 648)
EGFR-m879 Target: 5'-TCCAAGCTGTCCCAATGGAAGCTGCTG-3' (SEQ ID NO: 1004)

5'-CUGUGCCCAGCAAUGUCCCCAUCGCUG-3' (SEQ ID NO: 2429)
3'-GACACGGGUCGUUACAAGGGUAGCGAC-5' (SEQ ID NO: 649)
EGFR-m948 Target: 5'-CTGTGCCCAGCAATGTTCCCATCGCTG-3' (SEQ ID NO: 1005)

5'-GGAAGUACAGCUUUGGUGCCACCUGUG-3' (SEQ ID NO: 2430)
3'-CCUUAUGUCGAAACCACGGUGGACAC-5' (SEQ ID NO: 650)
EGFR-m1154 Target: 5'-GGAAGTACAGCTTTGGTGCCACCTGTG-3' (SEQ ID NO: 1006)

5'-CUGUCGCAAAGUUUGUAAUGGCAUAGG-3' (SEQ ID NO: 2431)
3'-GACAGCGUUUCAAACAUUACCGUAUCC-5' (SEQ ID NO: 651)
EGFR-m1302 Target: 5'-CTGTCGCAAAGTTTGTAATGGCATAGG-3' (SEQ ID NO: 1007)

5'-GGGAUUCUUUCACGCGCACUCCUCCUC-3' (SEQ ID NO: 2432)
3'-CCCUAAGAAAGUGCGCGUGAGGAGGAG-5' (SEQ ID NO: 652)
EGFR-m1439 Target: 5'-GGGATTCTTTACGCGCACTCCTCCTC-3' (SEQ ID NO: 1008)

5'-AACAGGCUUUUUGCUGAUUCAGGCUUG-3' (SEQ ID NO: 2433)
3'-UUGUCCGAAAAACGACUAAGUCCGAAC-5' (SEQ ID NO: 653)
EGFR-m1509 Target: 5'-AACAGGCTTTTTGCTGATTCAAGGCTTG-3' (SEQ ID NO: 1009)

5'-UUCAGGCUUGGCCUGAUAAACUGGACUG-3' (SEQ ID NO: 2434)
3'-AAGUCCGAACCGGACUAUUGACCUGAC-5' (SEQ ID NO: 654)
EGFR-m1526 Target: 5'-TTCAGGCTTGGCCTGATAACTGGACTG-3' (SEQ ID NO: 1010)

5'-CAGGCUUGGCCUGAUAAACUGGACUGAC-3' (SEQ ID NO: 2435)
3'-GUCCGAACCGGACUAUUGACCUGACUG-5' (SEQ ID NO: 655)
EGFR-m1528 Target: 5'-CAGGCTTGGCCTGATAACTGGACTGAC-3' (SEQ ID NO: 1011)

5'-GCUUGGCCUGAUAAACUGGACUGACCUC-3' (SEQ ID NO: 2436)
3'-CGAACCGGACUAUUGACCUGACUGGAG-5' (SEQ ID NO: 656)
EGFR-m1531 Target: 5'-GCTTGGCCTGATAACTGGACTGACCTC-3' (SEQ ID NO: 1012)

5'-ACGCCAACUGUACCUAUGGAUGUGCUG-3' (SEQ ID NO: 2437)
3'-UGCGGUUGACAUGGAUACCUACACGAC-5' (SEQ ID NO: 657)
EGFR-m2168 Target: 5'-ACGCCAACTGTACCTATGGATGTGCTG-3' (SEQ ID NO: 1013)

5'-CACUGGGAUUGUGGGUGGCCUCCUCUU-3' (SEQ ID NO: 2438)
3'-GUGACCCUAAACACCCACCGGAGGAGAA-5' (SEQ ID NO: 658)
EGFR-m2253 Target: 5'-CACTGGGATTGTGGGTGGCCTCCTCTT-3' (SEQ ID NO: 1014)

5'-GGUGGUGGCCCCUUGGGAUUGGCCUAUU-3' (SEQ ID NO: 2439)
3'-CCACCACCGGGAACCCUAAACCGGAUAA-5' (SEQ ID NO: 659)
EGFR-m2286 Target: 5'-GGTGGTGGCCCTTGGGATTGCCTATT-3' (SEQ ID NO: 1015)

5'-GAUUGGCCUAUUAUGCGAAGACGUCA-3' (SEQ ID NO: 2440)
3'-CUAACCGGAUAAGUACGCUUCUGCAGU-5' (SEQ ID NO: 660)
EGFR-m2301 Target: 5'-GATTGGCCTATTTCATGCGAAGACGTCA-3' (SEQ ID NO: 1016)

5'-CGCCGCCUGCUUCAAGAGAGAGAGCUC-3' (SEQ ID NO: 2441)
3'-GCGGCGGACGAAGUUCUCUCUCUCGAG-5' (SEQ ID NO: 661)
EGFR-m2350 Target: 5'-CGCCGCCTGCTTCAAGAGAGAGAGCTC-3' (SEQ ID NO: 1017)

5'-GCCGCCUGCUUCAAGAGAGAGAGCUCG-3' (SEQ ID NO: 2442)
3'-CGGCGGACGAAGUUCUCUCUCUCGAGC-5' (SEQ ID NO: 662)
EGFR-m2351 Target: 5'-GCCGCCTGCTTCAAGAGAGAGAGCTCG-3' (SEQ ID NO: 1018)

5'-CCGCCUGCUUCAAGAGAGAGAGCUCGU-3' (SEQ ID NO: 2443)
3'-GGCGGACGAAGUUCUCUCUCUCGAGCA-5' (SEQ ID NO: 663)
EGFR-m2352 Target: 5'-CCGCCTGCTTCAAGAGAGAGAGCTCGT-3' (SEQ ID NO: 1019)

5'-GUGGACAACCCUCAUGUAUGCCGCCUC-3' (SEQ ID NO: 2444)
3'-CACCUGUUGGGAGUACAUACGGCGGAG-5' (SEQ ID NO: 664)
EGFR-m2617 Target: 5'-GTGGACAACCCTCATGTATGCCGCCTC-3' (SEQ ID NO: 1020)

5'-UGUAUGCCGCCUCCUGGGCAUCUGUCU-3' (SEQ ID NO: 2445)
3'-ACAUACGGCGGAGGACCCGUAGACAGA-5' (SEQ ID NO: 665)
EGFR-m2631 Target: 5'-TGTATGCCGCCTCCTGGGCATCTGTCT-3' (SEQ ID NO: 1021)

5'-CAGCUCAUGCCCUACGGUUGCCUCCUG-3' (SEQ ID NO: 2446)
3'-GUCCAGUACGGGAUGCCAACGGAGGAC-5' (SEQ ID NO: 666)
EGFR-m2683 Target: 5'-CAGCTCATGCCCTACGGTTGCCTCCTG-3' (SEQ ID NO: 1022)

5'-AGCUCAUGCCCCUACGGUUGCCUCCUGG-3' (SEQ ID NO: 2447)
3'-UCGAGUACGGGAUGCCAACGGAGGACC-5' (SEQ ID NO: 667)
EGFR-m2684 Target: 5'-AGCTCATGCCCTACGGTTGCCTCCTGG-3' (SEQ ID NO: 1023)

5'-GAUCGGCGUUUGGUGCACCGUGACUUG-3' (SEQ ID NO: 2448)
3'-CUAGCCGCAAACACGUGGCACUGAAC-5' (SEQ ID NO: 668)
EGFR-m2800 Target: 5'-GATCGGCGTTTGGTGCACCGTGACTTG-3' (SEQ ID NO: 1024)

5'-GCGUUUGGUGCACCGUGACUUGGCAGC-3' (SEQ ID NO: 2449)
3'-CGCAAACACGUGGCACUGAACCGUCG-5' (SEQ ID NO: 669)
EGFR-m2805 Target: 5'-GCGTTTGGTGCACCGTGACTTGGCAGC-3' (SEQ ID NO: 1025)

5'-UUGGGCUGGCCAAACUGCUUGGUGCUG-3' (SEQ ID NO: 2450)
3'-AACCCGACCGGUUUGACGAACCACGAC-5' (SEQ ID NO: 670)
EGFR-m2879 Target: 5'-TTGGGCTGGCCAAACTGCTTGGTGCTG-3' (SEQ ID NO: 1026)

5'-UGGGCUGGCCAAACUGCUUGGUGCUGA-3' (SEQ ID NO: 2451)
3'-ACCCGACCGGUUUGACGAACCACGACU-5' (SEQ ID NO: 671)
EGFR-m2880 Target: 5'-TGGGCTGGCCAAACTGCTTGGTGCTGA-3' (SEQ ID NO: 1027)

5'-GGCUGGCCAAACUGCUUGGUGCUGAAG-3' (SEQ ID NO: 2452)
3'-CCGACCGGUUUGACGAACCACGACUUC-5' (SEQ ID NO: 672)
EGFR-m2882 Target: 5'-GGCTGGCCAAACTGCTTGGTGCTGAAG-3' (SEQ ID NO: 1028)

5'-GCUGGCCAAACUGCUUGGUGCUGAAGA-3' (SEQ ID NO: 2453)
3'-CGACCGGUUUGACGAACCACGACUUCU-5' (SEQ ID NO: 673)
EGFR-m2883 Target: 5'-GCTGGCCAAACTGCTTGGTGCTGAAGA-3' (SEQ ID NO: 1029)

5'-GUCAAGUGCUGGAUGAUAGAUGCUGAU-3' (SEQ ID NO: 2454)
3'-CAGUUCACGACCUACUAUCUACGACUA-5' (SEQ ID NO: 674)
EGFR-m3154 Target: 5'-GTCAAGTGCTGGATGATAGATGCTGAT-3' (SEQ ID NO: 1030)

5'-UCAAGUGCUGGAUGAUAGAUGCUGAUA-3' (SEQ ID NO: 2455)
3'-AGUUCACGACCUACUAUCUACGACUAU-5' (SEQ ID NO: 675)
EGFR-m3155 Target: 5'-TCAAGTGCTGGATGATAGATGCTGATA-3' (SEQ ID NO: 1031)

5'-CAAGUGCUGGAUGAUAGAUGCUGAUAG-3' (SEQ ID NO: 2456)
3'-GUUCACGACCUACUAUCUACGACUAUC-5' (SEQ ID NO: 676)
EGFR-m3156 Target: 5'-CAAGTGCTGGATGATAGATGCTGATAG-3' (SEQ ID NO: 1032)

5'-AAGUGCUGGAUGAUAGAUGCUGAUAGC-3' (SEQ ID NO: 2457)
3'-UUCACGACCUACUAUCUACGACUAUCG-5' (SEQ ID NO: 677)
EGFR-m3157 Target: 5'-AAGTGCTGGATGATAGATGCTGATAGC-3' (SEQ ID NO: 1033)

5'-AGUGCUGGAUGAUAGAUGCUGAUAGCC-3' (SEQ ID NO: 2458)
3'-UCACGACCUACUAUCUACGACUAUCGG-5' (SEQ ID NO: 678)

EGFR-m3158 Target: 5'-AGTGCTGGATGATAGATGCTGATAGCC-3' (SEQ ID NO: 1034)

5'-GUGCUGGAUGAUAGAUGCUGAUAGCCG-3' (SEQ ID NO: 2459)

3'-CACGACCUACUAUCUACGACUAUCGGC-5' (SEQ ID NO: 679)

EGFR-m3159 Target: 5'-GTGCTGGATGATAGATGCTGATAGCCG-3' (SEQ ID NO: 1035)

5'-UGCUGGAUGAUAGAUGCUGAUAGCCGC-3' (SEQ ID NO: 2460)

3'-ACGACCUACUAUCUACGACUAUCGGCG-5' (SEQ ID NO: 680)

EGFR-m3160 Target: 5'-TGCTGGATGATAGATGCTGATAGCCGC-3' (SEQ ID NO: 1036)

5'-GCUGGAUGAUAGAUGCUGAUAGCCGCC-3' (SEQ ID NO: 2461)

3'-CGACCUACUAUCUACGACUAUCGGCGG-5' (SEQ ID NO: 681)

EGFR-m3161 Target: 5'-GCTGGATGATAGATGCTGATAGCCGCC-3' (SEQ ID NO: 1037)

5'-CUGGAUGAUAGAUGCUGAUAGCCGCCC-3' (SEQ ID NO: 2462)

3'-GACCUACUAUCUACGACUAUCGGCGGG-5' (SEQ ID NO: 682)

EGFR-m3162 Target: 5'-CTGGATGATAGATGCTGATAGCCGCCC-3' (SEQ ID NO: 1038)

5'-UGGAUGAUAGAUGCUGAUAGCCGCCCA-3' (SEQ ID NO: 2463)

3'-ACCUACUAUCUACGACUAUCGGCGGGU-5' (SEQ ID NO: 683)

EGFR-m3163 Target: 5'-TGGATGATAGATGCTGATAGCCGCCCA-3' (SEQ ID NO: 1039)

5'-AUGAUAGAUGCUGAUAGCCGCCCAAAG-3' (SEQ ID NO: 2464)

3'-UACUAUCUACGACUAUCGGCGGGUUUC-5' (SEQ ID NO: 684)

EGFR-m3166 Target: 5'-ATGATAGATGCTGATAGCCGCCCAAAG-3' (SEQ ID NO: 1040)

5'-GAUAGAUGCUGAUAGCCGCCCAAAGUU-3' (SEQ ID NO: 2465)

3'-CUAUCUACGACUAUCGGCGGGUUUCA-5' (SEQ ID NO: 685)

EGFR-m3168 Target: 5'-GATAGATGCTGATAGCCGCCCAAAGTT-3' (SEQ ID NO: 1041)

5'-GAGCUGCCGUGUCAAGAAGACGCCUU-3' (SEQ ID NO: 2466)

3'-CUCGACGGCACAGUUUCUUCUGCGGA-5' (SEQ ID NO: 686)

EGFR-m3474 Target: 5'-GAGCTGCCGTGTCAAAGAAGACGCCTT-3' (SEQ ID NO: 1042)

5'-AGCUGCCGUGUCAAGAAGACGCCUUC-3' (SEQ ID NO: 2467)

3'-UCGACGGCACAGUUUCUUCUGCGGAAG-5' (SEQ ID NO: 687)

EGFR-m3475 Target: 5'-AGCTGCCGTGTCAAAGAAGACGCCTTC-3' (SEQ ID NO: 1043)

5'-AAGACGCCUUCUUGCAGCGGUACAGCU-3' (SEQ ID NO: 2468)

3'-UUCUGCGGAAGAACGUCGCCAUGUCGA-5' (SEQ ID NO: 688)

EGFR-m3491 Target: 5'-AAGACGCCTTCTTGCAGCGGTACAGCT-3' (SEQ ID NO: 1044)

5'-AGACGCCUUCUUGCAGCGGUACAGCUC-3' (SEQ ID NO: 2469)

3'-UCUGCGGAAGAACGUCGCCAUGUCGAG-5' (SEQ ID NO: 689)

EGFR-m3492 Target: 5'-AGACGCCTTCTTGCAGCGGTACAGCTC-3' (SEQ ID NO: 1045)

5'-GACGCCUUCUUGCAGCGGUACAGCUCC-3' (SEQ ID NO: 2470)

3'-CUGCGGAAGAACGUCGCCAUGUCGAGG-5' (SEQ ID NO: 690)
EGFR-m3493 Target: 5'-GACGCCCTTCTTGCAGCGGTACAGCTCC-3' (SEQ ID NO: 1046)

5'-ACGCCUUCUUGCAGCGGUACAGCUCCG-3' (SEQ ID NO: 2471)
3'-UGCGGAAGAACGUCGCCAUGUCGAGGC-5' (SEQ ID NO: 691)
EGFR-m3494 Target: 5'-ACGCCCTTCTTGCAGCGGTACAGCTCCG-3' (SEQ ID NO: 1047)

5'-CGCCUUCUUGCAGCGGUACAGCUCCGA-3' (SEQ ID NO: 2472)
3'-GCGGAAGAACGUCGCCAUGUCGAGGCU-5' (SEQ ID NO: 692)
EGFR-m3495 Target: 5'-CGCCTTCTTGCAGCGGTACAGCTCCGA-3' (SEQ ID NO: 1048)

5'-GCCUUCUUGCAGCGGUACAGCUCCGAC-3' (SEQ ID NO: 2473)
3'-CGGAAGAACGUCGCCAUGUCGAGGCU-5' (SEQ ID NO: 693)
EGFR-m3496 Target: 5'-GCCTTCTTGCAGCGGTACAGCTCCGAC-3' (SEQ ID NO: 1049)

5'-CCUUCUUGCAGCGGUACAGCUCCGACC-3' (SEQ ID NO: 2474)
3'-GGAAGAACGUCGCCAUGUCGAGGCUGG-5' (SEQ ID NO: 694)
EGFR-m3497 Target: 5'-CCTTCTTGCAGCGGTACAGCTCCGACC-3' (SEQ ID NO: 1050)

5'-GACUGGCUUUAAAGCAUAACUCUGAUG-3' (SEQ ID NO: 2475)
3'-CUGACCGAAAUUCGUUAUUGAGACUAC-5' (SEQ ID NO: 695)
EGFR-m4056 Target: 5'-GACTGGCTTTAAAGCATAACTCTGATG-3' (SEQ ID NO: 1051)

5'-AAGUGGGCCUCUCUCCUGAUGCACUUU-3' (SEQ ID NO: 2476)
3'-UUCACCCGGAGAGAGGACUACGUGAAA-5' (SEQ ID NO: 696)
EGFR-m4103 Target: 5'-AAGTGGGCCTCTCTCCTGATGCACTTT-3' (SEQ ID NO: 1052)

5'-AGUGGGCCUCUCUCCUGAUGCACUUUG-3' (SEQ ID NO: 2477)
3'-UCACCCGGAGAGAGGACUACGUGAAAC-5' (SEQ ID NO: 697)
EGFR-m4104 Target: 5'-AGTGGGCCTCTCTCCTGATGCACTTTG-3' (SEQ ID NO: 1053)

5'-GUGGGCCUCUCUCCUGAUGCACUUUGG-3' (SEQ ID NO: 2478)
3'-CACCCGGAGAGAGGACUACGUGAAACC-5' (SEQ ID NO: 698)
EGFR-m4105 Target: 5'-GTGGGCCTCTCTCCTGATGCACTTTGG-3' (SEQ ID NO: 1054)

5'-UGGGCCUCUCUCCUGAUGCACUUUGGG-3' (SEQ ID NO: 2479)
3'-ACCCGGAGAGAGGACUACGUGAAACCC-5' (SEQ ID NO: 699)
EGFR-m4106 Target: 5'-TGGGCCTCTCTCCTGATGCACTTTGGG-3' (SEQ ID NO: 1055)

5'-GCCUCUCUCCUGAUGCACUUUGGGAAG-3' (SEQ ID NO: 2480)
3'-CGGAGAGAGGACUACGUGAAACCUUC-5' (SEQ ID NO: 700)
EGFR-m4109 Target: 5'-GCCTCTCTCCTGATGCACTTTGGGAAG-3' (SEQ ID NO: 1056)

5'-GAUUGAUGCACUCUUGUAGUCUGGUAC-3' (SEQ ID NO: 2481)
3'-CUAACUACGUGAGAACAUACAGACCAUG-5' (SEQ ID NO: 701)
EGFR-m4309 Target: 5'-GATTGATGCACTCTTGTAGTCTGGTAC-3' (SEQ ID NO: 1057)

5'-UAGACUCCUUCUAUGUUUUCUGUUUC-3' (SEQ ID NO: 2482)
3'-AUCUGAAGGAAGAUACAAAAGACAAAAG-5' (SEQ ID NO: 702)
EGFR-m4619 Target: 5'-TAGACTTCCTTCTATGTTTTCTGTTTC-3' (SEQ ID NO: 1058)

5'-CUUCUAUGUUUUCUGUUUCAUUGUUUU-3' (SEQ ID NO: 2483)
3'-GAAGAUACAAAAGACAAAGUAACAAAA-5' (SEQ ID NO: 703)
EGFR-m4627 Target: 5'-CTTCTATGTTTTCTGTTTCATTGTTTT-3' (SEQ ID NO: 1059)

5'-UAUGUUUUUCUCCUGGUAAACUGCAG-3' (SEQ ID NO: 2484)
3'-AUACAAAAGAAGGACCAUUUGACGUC-5' (SEQ ID NO: 704)
EGFR-m5006 Target: 5'-TATGTTTTTCTTCCTGGTAAACTGCAG-3' (SEQ ID NO: 1060)

5'-AUGUUUUUCUCCUGGUAAACUGCAGC-3' (SEQ ID NO: 2485)
3'-UACAAAAGAAGGACCAUUUGACGUCG-5' (SEQ ID NO: 705)
EGFR-m5007 Target: 5'-ATGTTTTTCTTCCTGGTAAACTGCAGC-3' (SEQ ID NO: 1061)

5'-UGUUUUUCUCCUGGUAAACUGCAGCC-3' (SEQ ID NO: 2486)
3'-ACAAAAGAAGGACCAUUUGACGUCGG-5' (SEQ ID NO: 706)
EGFR-m5008 Target: 5'-TGTTTTTCTTCCTGGTAAACTGCAGCC-3' (SEQ ID NO: 1062)

5'-UUUCUCCUGGUAAACUGCAGCCAAAC-3' (SEQ ID NO: 2487)
3'-AAAGAAGGACCAUUUGACGUCGGUUUG-5' (SEQ ID NO: 707)
EGFR-m5012 Target: 5'-TTTCTTCCTGGTAAACTGCAGCCAAAC-3' (SEQ ID NO: 1063)

5'-UUCGAUCUCCUAAUGCUGUGACCCUU-3' (SEQ ID NO: 2488)
3'-AAGCUAGAAGGAUUACGACACUGGGAA-5' (SEQ ID NO: 708)
EGFR-m5329 Target: 5'-TTCGATCTTCCTAATGCTGTGACCCTT-3' (SEQ ID NO: 1064)

5'-UCGAUCUCCUAAUGCUGUGACCCUUU-3' (SEQ ID NO: 2489)
3'-AGCUAGAAGGAUUACGACACUGGGAAA-5' (SEQ ID NO: 709)
EGFR-m5330 Target: 5'-TCGATCTTCCTAATGCTGTGACCCTTT-3' (SEQ ID NO: 1065)

5'-UUGUUGCUACUUAACUGUAAAUUU-3' (SEQ ID NO: 2490)
3'-AACACGAUGAAGUAUUGACAUUUAAA-5' (SEQ ID NO: 710)
EGFR-m5403 Target: 5'-TTGTTGCTACTTCATAACTGTAAATTT-3' (SEQ ID NO: 1066)

5'-GCUUGCAGCAUCCUCUGGUUCCUAAC-3' (SEQ ID NO: 2491)
3'-CGAACGUCGUAGGAGACCAAAGGAUUG-5' (SEQ ID NO: 711)
EGFR-m5638 Target: 5'-GCTTGACGATCCTCTGGTTTCCTAAC-3' (SEQ ID NO: 1067)

5'-CGUUGCAAGCCACUCUAACUGUAGCAA-3' (SEQ ID NO: 2492)
3'-GCAACGUUCGGUGAGAUUGACAUCGUU-5' (SEQ ID NO: 712)
EGFR-m5895 Target: 5'-CGTTGCAAGCCACTCTAACTGTAGCAA-3' (SEQ ID NO: 1068)

Within Tables 2-5 and 7-10 above, underlined residues indicate 2'-O-methyl residues, UPPER CASE indicates ribonucleotides, and lower case denotes deoxyribonucleotides. The DsiRNA agents of Tables 2-5 above are 25/27mer agents possessing a blunt end. The structures and/or modification patterning of the agents of Tables 2-5 and 7-10 above can be readily adapted to the above generic sequence structures, *e.g.*, the 3' overhang of the second strand can be extended or contracted, 2'-O-methylation of the second strand can be expanded towards the 5' end of the second strand, optionally at alternating sites, etc. Such further modifications are optional, as 25/27mer DsiRNAs with such modifications can also be readily designed from the above DsiRNA agents and are also expected to be functional inhibitors of EGFR expression. Similarly, the 27mer "blunt/fray" and "blunt/blunt" DsiRNA structures and/or modification patterns of the agents of of Tables 7-10 above can also be readily adapted to the above generic sequence structures, *e.g.*, for application of modification patterning of the antisense strand to such structures and/or adaptation of such sequences to the above generic structures.

In certain embodiments, 27mer DsiRNAs possessing independent strand lengths each of 27 nucleotides are designed and synthesized for targeting of the same sites within the EGFR transcript as the asymmetric "25/27" structures shown in Tables 2-5 herein. Exemplary "27/27" DsiRNAs are optionally designed with a "blunt/fray" structure as shown for the DsiRNAs of Tables 7-8 above, or with a "blunt/blunt" structure as shown for the DsiRNAs of Tables 9-10 above.

In certain embodiments, the dsRNA agents of the invention require, *e.g.*, at least 19, at least 20, at least 21, at least 22, at least 23, at least 24, at least 25 or at least 26 residues of the first strand to be complementary to corresponding residues of the second strand. In certain related embodiments, these first strand residues complementary to corresponding residues of the second strand are optionally consecutive residues.

By definition, "sufficiently complementary" (contrasted with, *e.g.*, "100% complementary") allows for one or more mismatches to exist between a dsRNA of the invention and the target RNA or cDNA sequence (*e.g.*, EGFR mRNA), provided that the dsRNA possesses complementarity sufficient to trigger the destruction of the target RNA by the RNAi machinery (*e.g.*, the RISC complex) or process. In certain embodiments, a "sufficiently complementary" dsRNA of the invention can harbor one, two, three or even four or more mismatches between the dsRNA sequence and the target RNA or cDNA sequence

(e.g., in certain such embodiments, the antisense strand of the dsRNA harbors one, two, three, four, five or even six or more mismatches when aligned with the target RNA or cDNA sequence). Additional consideration of the preferred location of such mismatches within certain dsRNAs of the instant invention is considered in greater detail below.

As used herein “DsiRNAm” refers to a DsiRNA having a “mismatch tolerant region” containing one, two, three or four mismatched base pairs of the duplex formed by the sense and antisense strands of the DsiRNA, where such mismatches are positioned within the DsiRNA at a location(s) lying between (and thus not including) the two terminal base pairs of either end of the DsiRNA. The mismatched base pairs are located within a “mismatch-tolerant region” which is defined herein with respect to the location of the projected Ago2 cut site of the corresponding target nucleic acid. The mismatch tolerant region is located “upstream of” the projected Ago2 cut site of the target strand. “Upstream” in this context will be understood as the 5’-most portion of the DsiRNAm duplex, where 5’ refers to the orientation of the sense strand of the DsiRNA duplex. Therefore, the mismatch tolerant region is upstream of the base on the sense (passenger) strand that corresponds to the projected Ago2 cut site of the target nucleic acid (see Figure 1); alternatively, when referring to the antisense (guide) strand of the DsiRNAm, the mismatch tolerant region can also be described as positioned downstream of the base that is complementary to the projected Ago2 cut site of the target nucleic acid, that is, the 3’-most portion of the antisense strand of the DsiRNAm (where position 1 of the antisense strand is the 5’ terminal nucleotide of the antisense strand, see Figure 1).

In one embodiment, for example with numbering as depicted in Figure 1, the mismatch tolerant region is positioned between and including base pairs 3-9 when numbered from the nucleotide starting at the 5’ end of the sense strand of the duplex. Therefore, a DsiRNAm of the invention possesses a single mismatched base pair at any one of positions 3, 4, 5, 6, 7, 8 or 9 of the sense strand of a right-hand extended DsiRNA (where position 1 is the 5’ terminal nucleotide of the sense strand and position 9 is the nucleotide residue of the sense strand that is immediately 5’ of the projected Ago2 cut site of the target EGFR RNA sequence corresponding to the sense strand sequence). In certain embodiments, for a DsiRNAm that possesses a mismatched base pair nucleotide at any of positions 3, 4, 5, 6, 7, 8 or 9 of the sense strand, the corresponding mismatched base pair nucleotide of the antisense strand not only forms a mismatched base pair with the DsiRNAm sense strand sequence, but also forms a mismatched base pair with a DsiRNAm target EGFR RNA sequence (thus,

complementarity between the antisense strand sequence and the sense strand sequence is disrupted at the mismatched base pair within the DsiRNAm, and complementarity is similarly disrupted between the antisense strand sequence of the DsiRNAm and the target EGFR RNA sequence). In alternative embodiments, the mismatch base pair nucleotide of the antisense strand of a DsiRNAm only form a mismatched base pair with a corresponding nucleotide of the sense strand sequence of the DsiRNAm, yet base pairs with its corresponding target EGFR RNA sequence nucleotide (thus, complementarity between the antisense strand sequence and the sense strand sequence is disrupted at the mismatched base pair within the DsiRNAm, yet complementarity is maintained between the antisense strand sequence of the DsiRNAm and the target EGFR RNA sequence).

A DsiRNAm of the invention that possesses a single mismatched base pair within the mismatch-tolerant region (mismatch region) as described above (*e.g.*, a DsiRNAm harboring a mismatched nucleotide residue at any one of positions 3, 4, 5, 6, 7, 8 or 9 of the sense strand) can further include one, two or even three additional mismatched base pairs. In preferred embodiments, these one, two or three additional mismatched base pairs of the DsiRNAm occur at position(s) 3, 4, 5, 6, 7, 8 and/or 9 of the sense strand (and at corresponding residues of the antisense strand). In one embodiment where one additional mismatched base pair is present within a DsiRNAm, the two mismatched base pairs of the sense strand can occur, *e.g.*, at nucleotides of both position 4 and position 6 of the sense strand (with mismatch also occurring at corresponding nucleotide residues of the antisense strand).

In DsiRNAm agents possessing two mismatched base pairs, mismatches can occur consecutively (*e.g.*, at consecutive positions along the sense strand nucleotide sequence). Alternatively, nucleotides of the sense strand that form mismatched base pairs with the antisense strand sequence can be interspersed by nucleotides that base pair with the antisense strand sequence (*e.g.*, for a DsiRNAm possessing mismatched nucleotides at positions 3 and 6, but not at positions 4 and 5, the mismatched residues of sense strand positions 3 and 6 are interspersed by two nucleotides that form matched base pairs with corresponding residues of the antisense strand). For example, two residues of the sense strand (located within the mismatch-tolerant region of the sense strand) that form mismatched base pairs with the corresponding antisense strand sequence can occur with zero, one, two, three, four or five matched base pairs located between these mismatched base pairs.

For certain DsiRNAm agents possessing three mismatched base pairs, mismatches can occur consecutively (*e.g.*, in a triplet along the sense strand nucleotide sequence). Alternatively, nucleotides of the sense strand that form mismatched base pairs with the antisense strand sequence can be interspersed by nucleotides that form matched base pairs with the antisense strand sequence (*e.g.*, for a DsiRNAm possessing mismatched nucleotides at positions 3, 4 and 8, but not at positions 5, 6 and 7, the mismatched residues of sense strand positions 3 and 4 are adjacent to one another, while the mismatched residues of sense strand positions 4 and 8 are interspersed by three nucleotides that form matched base pairs with corresponding residues of the antisense strand). For example, three residues of the sense strand (located within the mismatch-tolerant region of the sense strand) that form mismatched base pairs with the corresponding antisense strand sequence can occur with zero, one, two, three or four matched base pairs located between any two of these mismatched base pairs.

For certain DsiRNAm agents possessing four mismatched base pairs, mismatches can occur consecutively (*e.g.*, in a quadruplet along the sense strand nucleotide sequence). Alternatively, nucleotides of the sense strand that form mismatched base pairs with the antisense strand sequence can be interspersed by nucleotides that form matched base pairs with the antisense strand sequence (*e.g.*, for a DsiRNAm possessing mismatched nucleotides at positions 3, 5, 7 and 8, but not at positions 4 and 6, the mismatched residues of sense strand positions 7 and 8 are adjacent to one another, while the mismatched residues of sense strand positions 3 and 5 are interspersed by one nucleotide that forms a matched base pair with the corresponding residue of the antisense strand – similarly, the the mismatched residues of sense strand positions 5 and 7 are also interspersed by one nucleotide that forms a matched base pair with the corresponding residue of the antisense strand). For example, four residues of the sense strand (located within the mismatch-tolerant region of the sense strand) that form mismatched base pairs with the corresponding antisense strand sequence can occur with zero, one, two or three matched base pairs located between any two of these mismatched base pairs.

In another embodiment, for example with numbering also as depicted in Figure 1, a DsiRNAm of the invention comprises a mismatch tolerant region which possesses a single mismatched base pair nucleotide at any one of positions 17, 18, 19, 20, 21, 22 or 23 of the antisense strand of the DsiRNA (where position 1 is the 5' terminal nucleotide of the antisense strand and position 17 is the nucleotide residue of the antisense strand that is

immediately 3' (downstream) in the antisense strand of the projected Ago2 cut site of the target EGFR RNA sequence sufficiently complementary to the antisense strand sequence). In certain embodiments, for a DsiRNAm that possesses a mismatched base pair nucleotide at any of positions 17, 18, 19, 20, 21, 22 or 23 of the antisense strand with respect to the sense strand of the DsiRNAm, the mismatched base pair nucleotide of the antisense strand not only forms a mismatched base pair with the DsiRNAm sense strand sequence, but also forms a mismatched base pair with a DsiRNAm target EGFR RNA sequence (thus, complementarity between the antisense strand sequence and the sense strand sequence is disrupted at the mismatched base pair within the DsiRNAm, and complementarity is similarly disrupted between the antisense strand sequence of the DsiRNAm and the target EGFR RNA sequence). In alternative embodiments, the mismatch base pair nucleotide of the antisense strand of a DsiRNAm only forms a mismatched base pair with a corresponding nucleotide of the sense strand sequence of the DsiRNAm, yet base pairs with its corresponding target EGFR RNA sequence nucleotide (thus, complementarity between the antisense strand sequence and the sense strand sequence is disrupted at the mismatched base pair within the DsiRNAm, yet complementarity is maintained between the antisense strand sequence of the DsiRNAm and the target EGFR RNA sequence).

A DsiRNAm of the invention that possesses a single mismatched base pair within the mismatch-tolerant region as described above (*e.g.*, a DsiRNAm harboring a mismatched nucleotide residue at positions 17, 18, 19, 20, 21, 22 or 23 of the antisense strand) can further include one, two or even three additional mismatched base pairs. In preferred embodiments, these one, two or three additional mismatched base pairs of the DsiRNAm occur at position(s) 17, 18, 19, 20, 21, 22 and/or 23 of the antisense strand (and at corresponding residues of the sense strand). In one embodiment where one additional mismatched base pair is present within a DsiRNAm, the two mismatched base pairs of the antisense strand can occur, *e.g.*, at nucleotides of both position 18 and position 20 of the antisense strand (with mismatch also occurring at corresponding nucleotide residues of the sense strand).

In DsiRNAm agents possessing two mismatched base pairs, mismatches can occur consecutively (*e.g.*, at consecutive positions along the antisense strand nucleotide sequence). Alternatively, nucleotides of the antisense strand that form mismatched base pairs with the sense strand sequence can be interspersed by nucleotides that base pair with the sense strand sequence (*e.g.*, for a DsiRNAm possessing mismatched nucleotides at positions 17 and 20, but not at positions 18 and 19, the mismatched residues of antisense strand positions 17 and

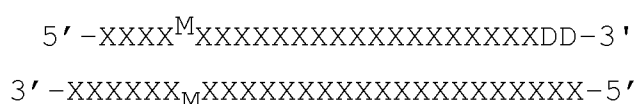
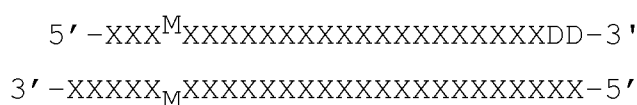
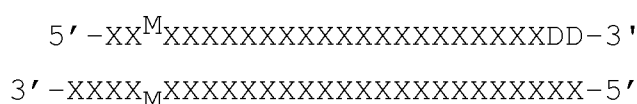
20 are interspersed by two nucleotides that form matched base pairs with corresponding residues of the sense strand). For example, two residues of the antisense strand (located within the mismatch-tolerant region of the sense strand) that form mismatched base pairs with the corresponding sense strand sequence can occur with zero, one, two, three, four, five, six or seven matched base pairs located between these mismatched base pairs.

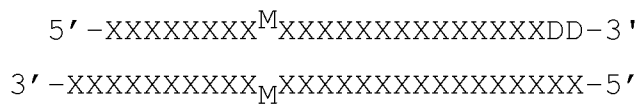
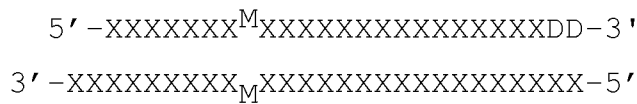
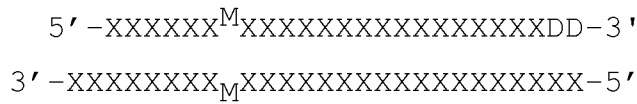
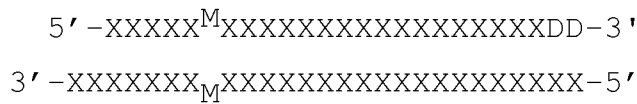
For certain DsiRNAm agents possessing three mismatched base pairs, mismatches can occur consecutively (*e.g.*, in a triplet along the antisense strand nucleotide sequence). Alternatively, nucleotides of the antisense strand that form mismatched base pairs with the sense strand sequence can be interspersed by nucleotides that form matched base pairs with the sense strand sequence (*e.g.*, for a DsiRNAm possessing mismatched nucleotides at positions 17, 18 and 22, but not at positions 19, 20 and 21, the mismatched residues of antisense strand positions 17 and 18 are adjacent to one another, while the mismatched residues of antisense strand positions 18 and 22 are interspersed by three nucleotides that form matched base pairs with corresponding residues of the sense strand). For example, three residues of the antisense strand (located within the mismatch-tolerant region of the antisense strand) that form mismatched base pairs with the corresponding sense strand sequence can occur with zero, one, two, three, four, five or six matched base pairs located between any two of these mismatched base pairs.

For certain DsiRNAm agents possessing four mismatched base pairs, mismatches can occur consecutively (*e.g.*, in a quadruplet along the antisense strand nucleotide sequence). Alternatively, nucleotides of the antisense strand that form mismatched base pairs with the sense strand sequence can be interspersed by nucleotides that form matched base pairs with the sense strand sequence (*e.g.*, for a DsiRNAm possessing mismatched nucleotides at positions 18, 20, 22 and 23, but not at positions 19 and 21, the mismatched residues of antisense strand positions 22 and 23 are adjacent to one another, while the mismatched residues of antisense strand positions 18 and 20 are interspersed by one nucleotide that forms a matched base pair with the corresponding residue of the sense strand – similarly, the mismatched residues of antisense strand positions 20 and 22 are also interspersed by one nucleotide that forms a matched base pair with the corresponding residue of the sense strand). For example, four residues of the antisense strand (located within the mismatch-tolerant region of the antisense strand) that form mismatched base pairs with the corresponding sense strand sequence can occur with zero, one, two, three, four or five matched base pairs located between any two of these mismatched base pairs.

For reasons of clarity, the location(s) of mismatched nucleotide residues within the above DsiRNAm agents are numbered in reference to the 5' terminal residue of either sense or antisense strands of the DsiRNAm. The numbering of positions located within the mismatch-tolerant region (mismatch region) of the antisense strand can shift with variations in the proximity of the 5' terminus of the sense or antisense strand to the projected Ago2 cleavage site. Thus, the location(s) of preferred mismatch sites within either antisense strand or sense strand can also be identified as the permissible proximity of such mismatches to the projected Ago2 cut site. Accordingly, in one preferred embodiment, the position of a mismatch nucleotide of the sense strand of a DsiRNAm is the nucleotide residue of the sense strand that is located immediately 5' (upstream) of the projected Ago2 cleavage site of the corresponding target EGFR RNA sequence. In other preferred embodiments, a mismatch nucleotide of the sense strand of a DsiRNAm is positioned at the nucleotide residue of the sense strand that is located two nucleotides 5' (upstream) of the projected Ago2 cleavage site, three nucleotides 5' (upstream) of the projected Ago2 cleavage site, four nucleotides 5' (upstream) of the projected Ago2 cleavage site, five nucleotides 5' (upstream) of the projected Ago2 cleavage site, six nucleotides 5' (upstream) of the projected Ago2 cleavage site, seven nucleotides 5' (upstream) of the projected Ago2 cleavage site, eight nucleotides 5' (upstream) of the projected Ago2 cleavage site, or nine nucleotides 5' (upstream) of the projected Ago2 cleavage site.

Exemplary single mismatch-containing 25/27mer DsiRNAs (DsiRNAm) include the following structures (such mismatch-containing structures may also be incorporated into other exemplary DsiRNA structures shown herein).





wherein “X”=RNA, “D”=DNA and “M”=Nucleic acid residues (RNA, DNA or non-natural or modified nucleic acids) that do not base pair (hydrogen bond) with corresponding “M” residues of otherwise complementary strand when strands are annealed. Any of the residues of such agents can optionally be 2'-O-methyl RNA monomers – alternating positioning of 2'-O-methyl RNA monomers that commences from the 3'-terminal residue of the bottom (second) strand, as shown above, can also be used in the above DsiRNAm agents. For the above mismatch structures, the top strand is the sense strand, and the bottom strand is the antisense strand.

In certain embodiments, a DsiRNA of the invention can contain mismatches that exist in reference to the target EGFR RNA sequence yet do not necessarily exist as mismatched base pairs within the two strands of the DsiRNA – thus, a DsiRNA can possess perfect complementarity between first and second strands of a DsiRNA, yet still possess mismatched residues in reference to a target EGFR RNA (which, in certain embodiments, may be advantageous in promoting efficacy and/or potency and/or duration of effect). In certain embodiments, where mismatches occur between antisense strand and target EGFR RNA sequence, the position of a mismatch is located within the antisense strand at a position(s) that corresponds to a sequence of the sense strand located 5' of the projected Ago2 cut site of the target region – *e.g.*, antisense strand residue(s) positioned within the antisense strand to

the 3' of the antisense residue which is complementary to the projected Ago2 cut site of the target sequence.

Exemplary 25/27mer DsiRNAs that harbor a single mismatched residue in reference to target sequences include the following structures.

Target RNA Sequence: 5'- . . . AXXXXXXXXXXXXXXXXXXXXX . . . -3'

DsiRNAm Sense Strand: 5'-XXXXXXXXXXXXXXXXXXXXDD-3'

DsiRNAm Antisense Strand: 3'-XXXXXXXXXXXXXXXXXXXXX-5'

Target RNA Sequence: 5'- . . . XXXXXXXXXXXXXXXXXXXXXX . . . -3'

DsiRNAm Sense Strand: 5'-XXXXXXXXXXXXXXXXXXXXDD-3'

DsiRNAm Antisense Strand: 3'-XXXXXXXXXXXXXXXXXXXXX-5'

Target RNA Sequence: 5'- . . . AXXXXXXXXXXXXXXXXXXXXX . . . -3'

DsiRNAm Sense Strand: 5'-BXXXXXXXXXXXXXXXXXXXXDD-3'

DsiRNAm Antisense Strand: 3'-XXXXXXXXXXXXXXXXXXXXX-5'

Target RNA Sequence: 5'- . . . XXXXXXXXXXXXXXXXXXXXXX . . . -3'

DsiRNAm Sense Strand: 5'-XBXXXXXXXXXXXXXXXXXXXXDD-3'

DsiRNAm Antisense Strand: 3'-XXXXXXXXXXXXXXXXXXXXXXXX-5'

Target RNA Sequence: 5'- . . . XXXXXXXXXXXXXXXXXXXXXXX . . . -3'

DsiRNAm Sense Strand: 5'-XXBXXXXXXXXXXXXXXXXXXXXDD-3'

DsiRNAm Antisense Strand: 3'-XXXXXXXXXXXXXXXXXXXXXXXXX-5'

Target RNA Sequence: 5'- . . . XXXXXXXXXXXXXXXXXXXXXXXX . . . -3'

DsiRNAm Sense Strand: 5'-XXXBXXXXXXXXXXXXXXXXXXXXDD-3'

DsiRNAm Antisense Strand: 3'-XXXXXXXXXXXXXXXXXXXXXXXXXX-5'

Target RNA Sequence: 5'- . . . XXXXAXXXXXXXXXXXXXXXXXX . . . -3'

DsiRNAm Sense Strand: 5'-XXXXBXXXXXXXXXXXXXXXXXXXXDD-3'

DsiRNAm Antisense Strand: 3'-XXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

Target RNA Sequence: 5'- . . . XXXXXAXXXXXXXXXXXXXXXXXX . . . -3'

DsiRNAm Sense Strand: 5'-XXXXXBXXXXXXXXXXXXXXXXXXXXDD-3'

DsiRNAm Antisense Strand: 3'-XXXXXXXXXXXXXXXXXXXXXXXXXXXX-5'

Target RNA Sequence: 5'-. . . XXXXXXXXAXXXXXXXXXXXXXX . . .-3'
 DsiRNAm Sense Strand: 5'-XXXXXXXXBXXXXXXXXXXXXXXXXXXXXDD-3'
 DsiRNAm Antisense Strand: 3'-XXXXXXXXXXEXXXXXXXXXXXXXXXXXXXXX-5'

Target RNA Sequence: 5'-. . . XXXXXXXXAXXXXXXXXXXXXXX . . .-3'
 DsiRNAm Sense Strand: 5'-XXXXXXXXBXXXXXXXXXXXXXXXXXXXXDD-3'
 DsiRNAm Antisense Strand: 3'-XXXXXXXXXXEXXXXXXXXXXXXXXXXXXXXX-5'

Target RNA Sequence: 5'-. . . XXXXXXXXAXXXXXXXXXXXXXX . . .-3'
 DsiRNAm Sense Strand: 5'-XXXXXXXXBXXXXXXXXXXXXXXXXXXXXDD-3'
 DsiRNAm Antisense Strand: 3'-XXXXXXXXXXEXXXXXXXXXXXXXXXXXXXXX-5'

wherein “X”=RNA, “D”=DNA and “E”=Nucleic acid residues (RNA, DNA or non-natural or modified nucleic acids) that do not base pair (hydrogen bond) with corresponding “A” RNA residues of otherwise complementary (target) strand when strands are annealed, yet optionally do base pair with corresponding “B” residues (“B” residues are also RNA, DNA or non-natural or modified nucleic acids). Any of the residues of such agents can optionally be 2'-O-methyl RNA monomers – alternating positioning of 2'-O-methyl RNA monomers that commences from the 3'-terminal residue of the bottom (second) strand, as shown above, can also be used in the above DsiRNA agents.

In certain embodiments, the guide strand of a dsRNA of the invention that is sufficiently complementary to a target RNA (*e.g.*, mRNA) along at least 19 nucleotides of the target gene sequence to reduce target gene expression is not perfectly complementary to the at least 19 nucleotide long target gene sequence. Rather, it is appreciated that the guide strand of a dsRNA of the invention that is sufficiently complementary to a target mRNA along at least 19 nucleotides of a target RNA sequence to reduce target gene expression can have one, two, three, or even four or more nucleotides that are mismatched with the 19 nucleotide or longer target strand sequence. Thus, for a 19 nucleotide target RNA sequence, the guide strand of a dsRNA of the invention can be sufficiently complementary to the target RNA sequence to reduce target gene levels while possessing, *e.g.*, only 15/19, 16/19, 17/19 or 18/19 matched nucleotide residues between guide strand and target RNA sequence.

In addition to the above-exemplified structures, dsRNAs of the invention can also possess one, two or three additional residues that form further mismatches with the target

EGFR RNA sequence. Such mismatches can be consecutive, or can be interspersed by nucleotides that form matched base pairs with the target EGFR RNA sequence. Where interspersed by nucleotides that form matched base pairs, mismatched residues can be spaced apart from each other within a single strand at an interval of one, two, three, four, five, six, seven or even eight base paired nucleotides between such mismatch-forming residues.

As for the above-described DsiRNAm agents, a preferred location within dsRNAs (*e.g.*, DsiRNAs) for antisense strand nucleotides that form mismatched base pairs with target EGFR RNA sequence (yet may or may not form mismatches with corresponding sense strand nucleotides) is within the antisense strand region that is located 3' (downstream) of the antisense strand sequence which is complementary to the projected Ago2 cut site of the DsiRNA (*e.g.*, in Figure 1, the region of the antisense strand which is 3' of the projected Ago2 cut site is preferred for mismatch-forming residues and happens to be located at positions 17-23 of the antisense strand for the 25/27mer agent shown in Figure 1). Thus, in one embodiment, the position of a mismatch nucleotide (in relation to the target EGFR RNA sequence) of the antisense strand of a DsiRNAm is the nucleotide residue of the antisense strand that is located immediately 3' (downstream) within the antisense strand sequence of the projected Ago2 cleavage site of the corresponding target EGFR RNA sequence. In other preferred embodiments, a mismatch nucleotide of the antisense strand of a DsiRNAm (in relation to the target EGFR RNA sequence) is positioned at the nucleotide residue of the antisense strand that is located two nucleotides 3' (downstream) of the corresponding projected Ago2 cleavage site, three nucleotides 3' (downstream) of the corresponding projected Ago2 cleavage site, four nucleotides 3' (downstream) of the corresponding projected Ago2 cleavage site, five nucleotides 3' (downstream) of the corresponding projected Ago2 cleavage site, six nucleotides 3' (downstream) of the projected Ago2 cleavage site, seven nucleotides 3' (downstream) of the projected Ago2 cleavage site, eight nucleotides 3' (downstream) of the projected Ago2 cleavage site, or nine nucleotides 3' (downstream) of the projected Ago2 cleavage site.

In dsRNA agents possessing two mismatch-forming nucleotides of the antisense strand (where mismatch-forming nucleotides are mismatch forming in relation to target EGFR RNA sequence), mismatches can occur consecutively (*e.g.*, at consecutive positions along the antisense strand nucleotide sequence). Alternatively, nucleotides of the antisense strand that form mismatched base pairs with the target EGFR RNA sequence can be interspersed by nucleotides that base pair with the target EGFR RNA sequence (*e.g.*, for a

DsiRNA possessing mismatch-forming nucleotides at positions 17 and 20 (starting from the 5' terminus (position 1) of the antisense strand of the 25/27mer agent shown in Figure 1), but not at positions 18 and 19, the mismatched residues of sense strand positions 17 and 20 are interspersed by two nucleotides that form matched base pairs with corresponding residues of the target EGFR RNA sequence). For example, two residues of the antisense strand (located within the mismatch-tolerant region of the antisense strand) that form mismatched base pairs with the corresponding target EGFR RNA sequence can occur with zero, one, two, three, four or five matched base pairs (with respect to target EGFR RNA sequence) located between these mismatch-forming base pairs.

For certain dsRNAs possessing three mismatch-forming base pairs (mismatch-forming with respect to target EGFR RNA sequence), mismatch-forming nucleotides can occur consecutively (*e.g.*, in a triplet along the antisense strand nucleotide sequence). Alternatively, nucleotides of the antisense strand that form mismatched base pairs with the target EGFR RNA sequence can be interspersed by nucleotides that form matched base pairs with the target EGFR RNA sequence (*e.g.*, for a DsiRNA possessing mismatched nucleotides at positions 17, 18 and 22, but not at positions 19, 20 and 21, the mismatch-forming residues of antisense strand positions 17 and 18 are adjacent to one another, while the mismatch-forming residues of antisense strand positions 18 and 22 are interspersed by three nucleotides that form matched base pairs with corresponding residues of the target EGFR RNA). For example, three residues of the antisense strand (located within the mismatch-tolerant region of the antisense strand) that form mismatched base pairs with the corresponding target EGFR RNA sequence can occur with zero, one, two, three or four matched base pairs located between any two of these mismatch-forming base pairs.

For certain dsRNAs possessing four mismatch-forming base pairs (mismatch-forming with respect to target EGFR RNA sequence), mismatch-forming nucleotides can occur consecutively (*e.g.*, in a quadruplet along the sense strand nucleotide sequence). Alternatively, nucleotides of the antisense strand that form mismatched base pairs with the target EGFR RNA sequence can be interspersed by nucleotides that form matched base pairs with the target EGFR RNA sequence (*e.g.*, for a DsiRNA possessing mismatch-forming nucleotides at positions 17, 19, 21 and 22, but not at positions 18 and 20, the mismatch-forming residues of antisense strand positions 21 and 22 are adjacent to one another, while the mismatch-forming residues of antisense strand positions 17 and 19 are interspersed by one nucleotide that forms a matched base pair with the corresponding residue of the target

EGFR RNA sequence – similarly, the mismatch-forming residues of antisense strand positions 19 and 21 are also interspersed by one nucleotide that forms a matched base pair with the corresponding residue of the target EGFR RNA sequence). For example, four residues of the antisense strand (located within the mismatch-tolerant region of the antisense strand) that form mismatched base pairs with the corresponding target EGFR RNA sequence can occur with zero, one, two or three matched base pairs located between any two of these mismatch-forming base pairs.

The above DsiRNAm and other dsRNA structures are described in order to exemplify certain structures of DsiRNAm and dsRNA agents. Design of the above DsiRNAm and dsRNA structures can be adapted to generate, *e.g.*, DsiRNAm forms of other DsiRNA structures shown *infra*. As exemplified above, dsRNAs can also be designed that possess single mismatches (or two, three or four mismatches) between the antisense strand of the dsRNA and a target sequence, yet optionally can retain perfect complementarity between sense and antisense strand sequences of a dsRNA.

It is further noted that the dsRNA agents exemplified *infra* can also possess insertion/deletion (in/del) structures within their double-stranded and/or target EGFR RNA-aligned structures. Accordingly, the dsRNAs of the invention can be designed to possess in/del variations in, *e.g.*, antisense strand sequence as compared to target EGFR RNA sequence and/or antisense strand sequence as compared to sense strand sequence, with preferred location(s) for placement of such in/del nucleotides corresponding to those locations described above for positioning of mismatched and/or mismatch-forming base pairs.

It is also noted that the DsiRNAs of the instant invention can tolerate mismatches within the 3'-terminal region of the sense strand/5'-terminal region of the antisense strand, as this region is modeled to be processed by Dicer and liberated from the guide strand sequence that loads into RISC. Exemplary DsiRNA structures of the invention that harbor such mismatches include the following:

Target RNA Sequence: 5'-. . . XXXXXXXXXXXXXXXXXXXXXXXHXXX . . . -3'

DsiRNA Sense Strand: 5'-XXXXXXXXXXXXXXXXXXXXIXDD-3'

DsiRNA Antisense Strand: 3'-XXXXXXXXXXXXXXXXXXXXJXXX-5'

Target RNA Sequence: 5'-. . . XXXXXXXXXXXXXXXXXXXXXXXHXX . . . -

3'

DsiRNA Sense Strand: 5'-XXXXXXXXXXXXXXXXXXXXXXXXXIDD-3'

DsiRNA Antisense Strand: 3'-XXXXXXXXXXXXXXXXXXXXXXXXXJXX-5'

Target RNA Sequence: 5'- . . . XXXXXXXXXXXXXXXXXXXXXXXXHX . . . -
3'

DsiRNA Sense Strand: 5'-XXXXXXXXXXXXXXXXXXXXXXXXXID-3'

DsiRNA Antisense Strand: 3'-XXXXXXXXXXXXXXXXXXXXXXXXXJX-5'

Target RNA Sequence: 5'- . . . XXXXXXXXXXXXXXXXXXXXXXXXH . . . -
3'

DsiRNA Sense Strand: 5'-XXXXXXXXXXXXXXXXXXXXXXXXXDI-3'

DsiRNA Antisense Strand: 3'-XXXXXXXXXXXXXXXXXXXXXXXXXJ-5'

wherein “X”=RNA, “D”=DNA and “I” and “J”=Nucleic acid residues (RNA, DNA or non-natural or modified nucleic acids) that do not base pair (hydrogen bond) with one another, yet optionally “J” is complementary to target RNA sequence nucleotide “H”. Any of the residues of such agents can optionally be 2'-O-methyl RNA monomers – alternating positioning of 2'-O-methyl RNA monomers that commences from the 3'-terminal residue of the bottom (second) strand, as shown above – or any of the above-described methylation patterns – can also be used in the above DsiRNA agents. The above mismatches can also be combined within the DsiRNAs of the instant invention.

In the below structures, such mismatches are introduced within the asymmetric EGFR-4249 DsiRNA (newly-introduced mismatch residues are *italicized*):

EGFR-4249 25/27mer DsiRNA, mismatch position = 22 of sense strand (from 5'-terminus)

5'-CUAUUGAUUUUUACUUCAUG^AGct-3' (SEQ ID NO: 2497)
3'-GCGAUAACUAAAAUGAAGUUAC_CCGA-5' (SEQ ID NO: 437)

Optionally, the mismatched “A” residue of position 22 of the sense strand is alternatively “U” or “C”.

EGFR-4249 25/27mer DsiRNA, mismatch position = 23 of sense strand

5'-CUAUUGAUUUUUACUUCAGG^Act-3' (SEQ ID NO: 2498)

3' - GCGAUAACUAAAAAUGAAGUUACCC_CGA-5' (SEQ ID NO: 437)

Optionally, the mismatched "A" residue of position 23 of the sense strand is alternatively "C" or "U".

EGFR-4249 25/27mer DsiRNA, mismatch position = 24 of sense strand

5' -CUAUUGAUUUUUACUUC^aAAUGGG^t-3' (SEQ ID NO: 2499)

3' - GCGAUAACUAAAAAUGAAGUUACCC_GA-5' (SEQ ID NO: 437)

Optionally, the mismatched "a" residue of position 24 of the sense strand is alternatively "g" or "t".

EGFR-4249 25/27mer DsiRNA, mismatch position = 25 of sense strand

5' -CUAUUGAUUUUUACUUC^aAAUGGG^aC-3' (SEQ ID NO: 2500)

3' - GCGAUAACUAAAAAUGAAGUUACCC_GA-5' (SEQ ID NO: 437)

Optionally, the mismatched "c" residue of position 25 of the sense strand is alternatively "a" or "g".

EGFR-4249 25/27mer DsiRNA, mismatch position = 1 of antisense strand

5' -CUAUUGAUUUUUACUUC^aAAUGGG^t-3' (SEQ ID NO: 81)

3' - GCGAUAACUAAAAAUGAAGUUACCC_GC-5' (SEQ ID NO: 2501)

Optionally, the mismatched "C" residue of position 1 of the antisense strand is alternatively "G" or "U".

EGFR-4249 25/27mer DsiRNA, mismatch position = 2 of antisense strand

5' -CUAUUGAUUUUUACUUC^aAAUGGG^t-3' (SEQ ID NO: 81)

3' - GCGAUAACUAAAAAUGAAGUUACCC_CA-5' (SEQ ID NO: 2502)

Optionally, the mismatched "C" residue of position 2 of the antisense strand is alternatively "G" or "A".

EGFR-4249 25/27mer DsiRNA, mismatch position = 3 of antisense strand

5' -CUAUUGAUUUUUACUUC^aAAUGG^Gat-3' (SEQ ID NO: 81)

3' - GCGAUAACUAAAAAUGAAGUUACC_AGA-5' (SEQ ID NO: 2503)

Optionally, the mismatched “A” residue of position 3 of the antisense strand is alternatively “U” or “G”.

EGFR-4249 25/27mer DsiRNA, mismatch position = 4 of antisense strand

5' -CUAUUGAUUUUUACUUC^GAUG-3' (SEQ ID NO: 81)
 3' -GCGAUAACUAAAAAUGAAGUUAC_ACGA-5' (SEQ ID NO: 2504)

Optionally, the mismatched “A” residue of position 4 of the antisense strand is alternatively “U” or “G”.

As noted above, introduction of such mismatches can be performed upon any of the DsiRNAs described herein.

The mismatches of such DsiRNA structures can be combined to produce a DsiRNA possessing, *e.g.*, two, three or even four mismatches within the 3'-terminal four nucleotides of the sense strand/5'-terminal four nucleotides of the antisense strand.

Indeed, in view of the flexibility of sequences which can be incorporated into DsiRNAs at the 3'-terminal residues of the sense strand/5'-terminal residues of the antisense strand, in certain embodiments, the sequence requirements of an asymmetric DsiRNA of the instant invention can be represented as the following (minimalist) structure (shown for an exemplary EGFR-4249 DsiRNA sequence):

5' -CUAUUGAUUUUUACUUC^GAUGXXX[X]_n-3' (SEQ ID NO: 2505)
 3' -GCGAUAACUAAAAAUGAAGUUXXXXX[X]_n-5' (SEQ ID NO: 2506)

where n= 1 to 5, 1 to 10, 1 to 20, 1 to 30, 1 to 50, or 1 to 80 or more.

EGFR-4249 Target: 5' -CGCTATTGATTTTACTTCAAXXXXXX-3' (SEQ ID NO: 2507)

The EGFR target site may also be a site which is targeted by one or more of several oligonucleotides whose complementary target sites overlap with a stated target site. For example, for an exemplary EGFR-2463 DsiRNA, it is noted that certain DsiRNAs targeting overlapping and only slightly offset EGFR sequences can exhibit activity levels similar to that of EGFR-2463 (specifically, see EGFR-2460, EGFR-2461, EGFR-2462, EGFR-2464 and EGFR-2465 DsiRNAs of Table 11 below. Thus, in certain embodiments, a designated target sequence region can be effectively targeted by a series of DsiRNAs possessing largely overlapping sequences. (*E.g.*, if considering DsiRNAs surrounding the EGFR-2463 site, a

more encompassing EGFR target sequence might be recited as, *e.g.*, 5'-CTCTGGATCCCAGAAGGTGAGAAAGTTAAAAT-3' (SEQ ID NO: 2508), wherein any given DsiRNA (*e.g.*, a DsiRNA selected from EGFR-2460, EGFR-2461, EGFR-2462, EGFR-2463, EGFR-2464 and EGFR-2465) only targets a sub-sequence within such a sequence region, yet the entire sequence can be considered a viable target for such a series of DsiRNAs).

Additionally and/or alternatively, mismatches within the 3'-terminal four nucleotides of the sense strand/5'-terminal four nucleotides of the antisense strand can be combined with mismatches positioned at other mismatch-tolerant positions, as described above.

In view of the present identification of the above-described Dicer substrate agents (DsiRNAs) as inhibitors of EGFR levels *via* targeting of specific EGFR sequences, it is also recognized that dsRNAs having structures similar to those described herein can also be synthesized which target other sequences within the EGFR sequence of NM_005228.3 or NM_207655.2, or within variants thereof (*e.g.*, target sequences possessing 80% identity, 90% identity, 95% identity, 96% identity, 97% identity, 98% identity, 99% or more identity to a sequence of NM_005228.3 and/or NM_207655.2).

Anti-EGFR DsiRNA Design/Synthesis

It has been found empirically that longer dsRNA species of from 25 to 35 nucleotides (DsiRNAs) and especially from 25 to 30 nucleotides give unexpectedly effective results in terms of potency and duration of action, as compared to 19-23mer siRNA agents. Without wishing to be bound by the underlying theory of the dsRNA processing mechanism, it is thought that the longer dsRNA species serve as a substrate for the Dicer enzyme in the cytoplasm of a cell. In addition to cleaving the dsRNA of the invention into shorter segments, Dicer is thought to facilitate the incorporation of a single-stranded cleavage product derived from the cleaved dsRNA into the RISC complex that is responsible for the destruction of the cytoplasmic RNA (*e.g.*, EGFR RNA) of or derived from the target gene, EGFR (or other gene associated with an EGFR-associated disease or disorder). Prior studies (Rossi *et al.*, U.S. Patent Application No. 2007/0265220) have shown that the cleavability of a dsRNA species (specifically, a DsiRNA agent) by Dicer corresponds with increased potency and duration of action of the dsRNA species.

Certain preferred anti-EGFR DsiRNA agents were selected from a pre-screened population. Design of DsiRNAs can optionally involve use of predictive scoring algorithms that perform *in silico* assessments of the projected activity/efficacy of a number of possible DsiRNA agents spanning a region of sequence. Information regarding the design of such scoring algorithms can be found, *e.g.*, in Gong *et al.* (*BMC Bioinformatics* 2006, 7:516), though a more recent “v3” algorithm represents a theoretically improved algorithm relative to siRNA scoring algorithms previously available in the art. (E.g., the “v3” and “v4” scoring algorithms are machine learning algorithms that are not reliant upon any biases in human sequence. In addition, the “v3” and “v4” algorithms derive from data sets that are many-fold larger than that from which an older “v2” algorithm such as that described in Gong *et al.* derives.)

The first and second oligonucleotides of the DsiRNA agents of the instant invention are not required to be completely complementary. In fact, in one embodiment, the 3'-terminus of the sense strand contains one or more mismatches. In one aspect, two mismatches are incorporated at the 3' terminus of the sense strand. In another embodiment, the DsiRNA of the invention is a double stranded RNA molecule containing two RNA oligonucleotides each of which is 27 nucleotides in length and, when annealed to each other, have blunt ends and a two nucleotide mismatch on the 3'-terminus of the sense strand (the 5'-terminus of the antisense strand). The use of mismatches or decreased thermodynamic stability (specifically at the 3'-sense/5'-antisense position) has been proposed to facilitate or favor entry of the antisense strand into RISC (Schwarz *et al.*, 2003, *Cell* 115: 199-208; Khvorova *et al.*, 2003, *Cell* 115: 209-216), presumably by affecting some rate-limiting unwinding steps that occur with entry of the siRNA into RISC. Thus, terminal base composition has been included in design algorithms for selecting active 21mer siRNA duplexes (Ui-Tei *et al.*, 2004, *Nucleic Acids Res* 32: 936-948; Reynolds *et al.*, 2004, *Nat Biotechnol* 22: 326-330). With Dicer cleavage of the dsRNA of this embodiment, the small end-terminal sequence which contains the mismatches will either be left unpaired with the antisense strand (become part of a 3'-overhang) or be cleaved entirely off the final 21-mer siRNA. These "mismatches", therefore, do not persist as mismatches in the final RNA component of RISC. The finding that base mismatches or destabilization of segments at the 3'-end of the sense strand of Dicer substrate improved the potency of synthetic duplexes in RNAi, presumably by facilitating processing by Dicer, was a surprising finding of past works

describing the design and use of 25-30mer dsRNAs (also termed “DsiRNAs” herein; Rossi *et al.*, U.S. Patent Application Nos. 2005/0277610, 2005/0244858 and 2007/0265220).

Modification of Anti-EGFR dsRNAs

One major factor that inhibits the effect of double stranded RNAs (“dsRNAs”) is the degradation of dsRNAs (*e.g.*, siRNAs and DsiRNAs) by nucleases. A 3'-exonuclease is the primary nuclease activity present in serum and modification of the 3'-ends of antisense DNA oligonucleotides is crucial to prevent degradation (Eder *et al.*, 1991, *Antisense Res Dev*, 1: 141-151). An RNase-T family nuclease has been identified called ERI-1 which has 3' to 5' exonuclease activity that is involved in regulation and degradation of siRNAs (Kennedy *et al.*, 2004, *Nature* 427: 645-649; Hong *et al.*, 2005, *Biochem J*, 390: 675-679). This gene is also known as Thex1 (NM_02067) in mice or THEX1 (NM_153332) in humans and is involved in degradation of histone mRNA; it also mediates degradation of 3'-overhangs in siRNAs, but does not degrade duplex RNA (Yang *et al.*, 2006, *J Biol Chem*, 281: 30447-30454). It is therefore reasonable to expect that 3'-end-stabilization of dsRNAs, including the DsiRNAs of the instant invention, will improve stability.

XRN1 (NM_019001) is a 5' to 3' exonuclease that resides in P-bodies and has been implicated in degradation of mRNA targeted by miRNA (Rehwinkel *et al.*, 2005, *RNA* 11: 1640-1647) and may also be responsible for completing degradation initiated by internal cleavage as directed by a siRNA. XRN2 (NM_012255) is a distinct 5' to 3' exonuclease that is involved in nuclear RNA processing.

RNase A is a major endonuclease activity in mammals that degrades RNAs. It is specific for ssRNA and cleaves at the 3'-end of pyrimidine bases. SiRNA degradation products consistent with RNase A cleavage can be detected by mass spectrometry after incubation in serum (Turner *et al.*, 2007, *Mol Biosyst* 3: 43-50). The 3'-overhangs enhance the susceptibility of siRNAs to RNase degradation. Depletion of RNase A from serum reduces degradation of siRNAs; this degradation does show some sequence preference and is worse for sequences having poly A/U sequence on the ends (Haupenthal *et al.*, 2006 *Biochem Pharmacol* 71: 702-710). This suggests the possibility that lower stability regions of the duplex may “breathe” and offer transient single-stranded species available for degradation by RNase A. RNase A inhibitors can be added to serum and improve siRNA longevity and potency (Haupenthal *et al.*, 2007, *Int J. Cancer* 121: 206-210).

In 21mers, phosphorothioate or boranophosphate modifications directly stabilize the internucleoside phosphate linkage. Boranophosphate modified RNAs are highly nuclease resistant, potent as silencing agents, and are relatively non-toxic. Boranophosphate modified RNAs cannot be manufactured using standard chemical synthesis methods and instead are made by in vitro transcription (IVT) (Hall *et al.*, 2004, *Nucleic Acids Res* 32: 5991-6000; Hall *et al.*, 2006, *Nucleic Acids Res* 34: 2773-2781). Phosphorothioate (PS) modifications can be easily placed in the RNA duplex at any desired position and can be made using standard chemical synthesis methods. The PS modification shows dose-dependent toxicity, so most investigators have recommended limited incorporation in siRNAs, favoring the 3'-ends where protection from nucleases is most important (Harborth *et al.*, 2003, *Antisense Nucleic Acid Drug Dev* 13: 83-105; Chiu and Rana, 2003, *Mol Cell* 10: 549-561; Braasch *et al.*, 2003, *Biochemistry* 42: 7967-7975; Amarzguoui *et al.*, 2003, *Nucleic Acids Research* 31: 589-595). More extensive PS modification can be compatible with potent RNAi activity; however, use of sugar modifications (such as 2'-O-methyl RNA) may be superior (Choung *et al.*, 2006, *Biochem Biophys Res Commun* 342: 919-927).

A variety of substitutions can be placed at the 2'-position of the ribose which generally increases duplex stability (T_m) and can greatly improve nuclease resistance. 2'-O-methyl RNA is a naturally occurring modification found in mammalian ribosomal RNAs and transfer RNAs. 2'-O-methyl modification in siRNAs is known, but the precise position of modified bases within the duplex is important to retain potency and complete substitution of 2'-O-methyl RNA for RNA will inactivate the siRNA. For example, a pattern that employs alternating 2'-O-methyl bases can have potency equivalent to unmodified RNA and is quite stable in serum (Choung *et al.*, 2006, *Biochem Biophys Res Commun* 342: 919-927; Czauderna *et al.*, 2003, *Nucleic Acids Research* 31: 2705-2716).

The 2'-fluoro (2'-F) modification is also compatible with dsRNA (*e.g.*, siRNA and DsiRNA) function; it is most commonly placed at pyrimidine sites (due to reagent cost and availability) and can be combined with 2'-O-methyl modification at purine positions; 2'-F purines are available and can also be used. Heavily modified duplexes of this kind can be potent triggers of RNAi in vitro (Allerson *et al.*, 2005, *J Med Chem* 48: 901-904; Prakash *et al.*, 2005, *J Med Chem* 48: 4247-4253; Kraynack and Baker, 2006, *RNA* 12: 163-176) and can improve performance and extend duration of action when used in vivo (Morrissey *et al.*, 2005, *Hepatology* 41: 1349-1356; Morrissey *et al.*, 2005, *Nat Biotechnol* 23: 1002-1007). A highly potent, nuclease stable, blunt 19mer duplex containing alternative 2'-F and 2'-O-Me

bases is taught by Allerson. In this design, alternating 2'-O-Me residues are positioned in an identical pattern to that employed by Czauderna, however the remaining RNA residues are converted to 2'-F modified bases. A highly potent, nuclease resistant siRNA employed by Morrissey employed a highly potent, nuclease resistant siRNA *in vivo*. In addition to 2'-O-Me RNA and 2'-F RNA, this duplex includes DNA, RNA, inverted abasic residues, and a 3'-terminal PS internucleoside linkage. While extensive modification has certain benefits, more limited modification of the duplex can also improve *in vivo* performance and is both simpler and less costly to manufacture. Soutschek *et al.* (2004, *Nature* 432: 173-178) employed a duplex *in vivo* and was mostly RNA with two 2'-O-Me RNA bases and limited 3'-terminal PS internucleoside linkages.

Locked nucleic acids (LNAs) are a different class of 2'-modification that can be used to stabilize dsRNA (*e.g.*, siRNA and DsiRNA). Patterns of LNA incorporation that retain potency are more restricted than 2'-O-methyl or 2'-F bases, so limited modification is preferred (Braasch *et al.*, 2003, *Biochemistry* 42: 7967-7975; Grunweller *et al.*, 2003, *Nucleic Acids Res* 31: 3185-3193; Elmen *et al.*, 2005, *Nucleic Acids Res* 33: 439-447). Even with limited incorporation, the use of LNA modifications can improve dsRNA performance *in vivo* and may also alter or improve off target effect profiles (Mook *et al.*, 2007, *Mol Cancer Ther* 6: 833-843).

Synthetic nucleic acids introduced into cells or live animals can be recognized as "foreign" and trigger an immune response. Immune stimulation constitutes a major class of off-target effects which can dramatically change experimental results and even lead to cell death. The innate immune system includes a collection of receptor molecules that specifically interact with DNA and RNA that mediate these responses, some of which are located in the cytoplasm and some of which reside in endosomes (Marques and Williams, 2005, *Nat Biotechnol* 23: 1399-1405; Schlee *et al.*, 2006, *Mol Ther* 14: 463-470). Delivery of siRNAs by cationic lipids or liposomes exposes the siRNA to both cytoplasmic and endosomal compartments, maximizing the risk for triggering a type 1 interferon (IFN) response both *in vitro* and *in vivo* (Morrissey *et al.*, 2005, *Nat Biotechnol* 23: 1002-1007; Sioud and Sorensen, 2003, *Biochem Biophys Res Commun* 312: 1220-1225; Sioud, 2005, *J Mol Biol* 348: 1079-1090; Ma *et al.*, 2005, *Biochem Biophys Res Commun* 330: 755-759). RNAs transcribed within the cell are less immunogenic (Robbins *et al.*, 2006, *Nat Biotechnol* 24: 566-571) and synthetic RNAs that are immunogenic when delivered using lipid-based methods can evade immune stimulation when introduced into cells by mechanical means,

even *in vivo* (Heidel *et al.*, 2004, *Nat Biotechnol* 22: 1579-1582). However, lipid based delivery methods are convenient, effective, and widely used. Some general strategy to prevent immune responses is needed, especially for *in vivo* application where all cell types are present and the risk of generating an immune response is highest. Use of chemically modified RNAs may solve most or even all of these problems.

In certain embodiments, modifications can be included in the anti-EGFR dsRNA agents of the present invention so long as the modification does not prevent the dsRNA agent from possessing EGFR inhibitory activity. In one embodiment, one or more modifications are made that enhance Dicer processing of the DsiRNA agent (an assay for determining Dicer processing of a DsiRNA is described elsewhere herein). In a second embodiment, one or more modifications are made that result in more effective EGFR inhibition (as described herein, EGFR inhibition/EGFR inhibitory activity of a dsRNA can be assayed *via* art-recognized methods for determining RNA levels, or for determining EGFR polypeptide levels, should such levels be assessed in lieu of or in addition to assessment of, *e.g.*, EGFR mRNA levels). In a third embodiment, one or more modifications are made that support greater EGFR inhibitory activity (means of determining EGFR inhibitory activity are described *supra*). In a fourth embodiment, one or more modifications are made that result in greater potency of EGFR inhibitory activity per each dsRNA agent molecule to be delivered to the cell (potency of EGFR inhibitory activity is described *supra*). Modifications can be incorporated in the 3'-terminal region, the 5'-terminal region, in both the 3'-terminal and 5'-terminal region or in some instances in various positions within the sequence. With the restrictions noted above in mind, numbers and combinations of modifications can be incorporated into the dsRNA agent. Where multiple modifications are present, they may be the same or different. Modifications to bases, sugar moieties, the phosphate backbone, and their combinations are contemplated. Either 5'-terminus can be phosphorylated.

Examples of modifications contemplated for the phosphate backbone include phosphonates, including methylphosphonate, phosphorothioate, and phosphotriester modifications such as alkylphosphotriesters, and the like. Examples of modifications contemplated for the sugar moiety include 2'-alkyl pyrimidine, such as 2'-O-methyl, 2'-fluoro, amino, and deoxy modifications and the like (see, *e.g.*, Amarzguioui *et al.*, 2003, *Nucleic Acids Research* 31: 589-595). Examples of modifications contemplated for the base groups include abasic sugars, 2-O-alkyl modified pyrimidines, 4-thiouracil, 5-bromouracil, 5-iodouracil, and 5-(3-aminoallyl)-uracil and the like. Locked nucleic acids, or LNA's, could

also be incorporated. Many other modifications are known and can be used so long as the above criteria are satisfied. Examples of modifications are also disclosed in U.S. Pat. Nos. 5,684,143, 5,858,988 and 6,291,438 and in U.S. published patent application No.

2004/0203145 A1. Other modifications are disclosed in Herdewijn (2000, *Antisense Nucleic Acid Drug Dev* 10: 297-310), Eckstein (2000, *Antisense Nucleic Acid Drug Dev* 10: 117-21), Rusckowski *et al.* (2000, *Antisense Nucleic Acid Drug Dev* 10: 333-345), Stein *et al.* (2001, *Antisense Nucleic Acid Drug Dev* 11: 317-25); Vorobjev *et al.* (2001, *Antisense Nucleic Acid Drug Dev* 11: 77-85).

One or more modifications contemplated can be incorporated into either strand. The placement of the modifications in the dsRNA agent can greatly affect the characteristics of the dsRNA agent, including conferring greater potency and stability, reducing toxicity, enhance Dicer processing, and minimizing an immune response. In one embodiment, the antisense strand or the sense strand or both strands have one or more 2'-O-methyl modified nucleotides. In another embodiment, the antisense strand contains 2'-O-methyl modified nucleotides. In another embodiment, the antisense strand contains a 3' overhang that is comprised of 2'-O-methyl modified nucleotides. The antisense strand could also include additional 2'-O-methyl modified nucleotides.

In certain embodiments, the anti-EGFR DsiRNA agent of the invention has several properties which enhance its processing by Dicer. According to such embodiments, the DsiRNA agent has a length sufficient such that it is processed by Dicer to produce an siRNA and at least one of the following properties: (i) the DsiRNA agent is asymmetric, *e.g.*, has a 3' overhang on the sense strand and (ii) the DsiRNA agent has a modified 3' end on the antisense strand to direct orientation of Dicer binding and processing of the dsRNA to an active siRNA. According to these embodiments, the longest strand in the DsiRNA agent comprises 25-30 nucleotides. In one embodiment, the sense strand comprises 25-30 nucleotides and the antisense strand comprises 25-28 nucleotides. Thus, the resulting dsRNA has an overhang on the 3' end of the sense strand. The overhang is 1-4 nucleotides, such as 2 nucleotides. The antisense strand may also have a 5' phosphate.

In certain embodiments, the sense strand of a DsiRNA agent is modified for Dicer processing by suitable modifiers located at the 3' end of the sense strand, *i.e.*, the DsiRNA agent is designed to direct orientation of Dicer binding and processing. Suitable modifiers include nucleotides such as deoxyribonucleotides, dideoxyribonucleotides, acyclonucleotides and the like and sterically hindered molecules, such as fluorescent molecules and the like.

Acyclonucleotides substitute a 2-hydroxyethoxymethyl group for the 2'-deoxyribofuranosyl sugar normally present in dNMPs. Other nucleotide modifiers could include 3'-deoxyadenosine (cordycepin), 3'-azido-3'-deoxythymidine (AZT), 2',3'-dideoxyinosine (ddI), 2',3'-dideoxy-3'-thiacytidine (3TC), 2',3'-didehydro-2',3'-dideoxythymidine (d4T) and the monophosphate nucleotides of 3'-azido-3'-deoxythymidine (AZT), 2',3'-dideoxy-3'-thiacytidine (3TC) and 2',3'-didehydro-2',3'-dideoxythymidine (d4T). In one embodiment, deoxynucleotides are used as the modifiers. When nucleotide modifiers are utilized, 1-3 nucleotide modifiers, or 2 nucleotide modifiers are substituted for the ribonucleotides on the 3' end of the sense strand. When sterically hindered molecules are utilized, they are attached to the ribonucleotide at the 3' end of the antisense strand. Thus, the length of the strand does not change with the incorporation of the modifiers. In another embodiment, the invention contemplates substituting two DNA bases in the dsRNA to direct the orientation of Dicer processing. In a further invention, two terminal DNA bases are located on the 3' end of the sense strand in place of two ribonucleotides forming a blunt end of the duplex on the 5' end of the antisense strand and the 3' end of the sense strand, and a two-nucleotide RNA overhang is located on the 3'-end of the antisense strand. This is an asymmetric composition with DNA on the blunt end and RNA bases on the overhanging end.

In certain other embodiments, the antisense strand of a DsiRNA agent is modified for Dicer processing by suitable modifiers located at the 3' end of the antisense strand, *i.e.*, the DsiRNA agent is designed to direct orientation of Dicer binding and processing. Suitable modifiers include nucleotides such as deoxyribonucleotides, dideoxyribonucleotides, acyclonucleotides and the like and sterically hindered molecules, such as fluorescent molecules and the like. Acyclonucleotides substitute a 2-hydroxyethoxymethyl group for the 2'-deoxyribofuranosyl sugar normally present in dNMPs. Other nucleotide modifiers could include 3'-deoxyadenosine (cordycepin), 3'-azido-3'-deoxythymidine (AZT), 2',3'-dideoxyinosine (ddI), 2',3'-dideoxy-3'-thiacytidine (3TC), 2',3'-didehydro-2',3'-dideoxythymidine (d4T) and the monophosphate nucleotides of 3'-azido-3'-deoxythymidine (AZT), 2',3'-dideoxy-3'-thiacytidine (3TC) and 2',3'-didehydro-2',3'-dideoxythymidine (d4T). In one embodiment, deoxynucleotides are used as the modifiers. When nucleotide modifiers are utilized, 1-3 nucleotide modifiers, or 2 nucleotide modifiers are substituted for the ribonucleotides on the 3' end of the antisense strand. When sterically hindered molecules are utilized, they are attached to the ribonucleotide at the 3' end of the antisense strand. Thus, the length of the strand does not change with the incorporation of the modifiers. In another

embodiment, the invention contemplates substituting two DNA bases in the dsRNA to direct the orientation of Dicer processing. In a further invention, two terminal DNA bases are located on the 3' end of the antisense strand in place of two ribonucleotides forming a blunt end of the duplex on the 5' end of the sense strand and the 3' end of the antisense strand, and a two-nucleotide RNA overhang is located on the 3'-end of the sense strand. This is also an asymmetric composition with DNA on the blunt end and RNA bases on the overhanging end.

The sense and antisense strands anneal under biological conditions, such as the conditions found in the cytoplasm of a cell. In addition, a region of one of the sequences, particularly of the antisense strand, of the dsRNA has a sequence length of at least 15 (in certain embodiments, 19 nucleotides) nucleotides, wherein these nucleotides are adjacent to the 3' end of antisense strand and are sufficiently complementary to a nucleotide sequence of the target EGFR RNA.

Additionally, the DsiRNA agent structure can be optimized to ensure that the oligonucleotide segment generated from Dicer's cleavage will be the portion of the oligonucleotide that is most effective in inhibiting gene expression. For example, in one embodiment of the invention, a 27-bp oligonucleotide of the DsiRNA agent structure is synthesized wherein the anticipated 21 to 22-bp segment that will inhibit gene expression is located on the 3'-end of the antisense strand. The remaining bases located on the 5'-end of the antisense strand will be cleaved by Dicer and will be discarded. This cleaved portion can be homologous (*i.e.*, based on the sequence of the target sequence) or non-homologous and added to extend the nucleic acid strand.

US 2007/0265220 discloses that 27mer DsiRNAs show improved stability in serum over comparable 21mer siRNA compositions, even absent chemical modification. Modifications of DsiRNA agents, such as inclusion of 2'-O-methyl RNA in the antisense strand, in patterns such as detailed above, when coupled with addition of a 5' Phosphate, can improve stability of DsiRNA agents. Addition of 5'-phosphate to all strands in synthetic RNA duplexes may be an inexpensive and physiological method to confer some limited degree of nuclease stability.

The chemical modification patterns of the dsRNA agents of the instant invention are designed to enhance the efficacy of such agents. Accordingly, such modifications are designed to avoid reducing potency of dsRNA agents; to avoid interfering with Dicer processing of DsiRNA agents; to improve stability in biological fluids (reduce nuclease sensitivity) of dsRNA agents; or to block or evade detection by the innate immune system.

Such modifications are also designed to avoid being toxic and to avoid increasing the cost or impact the ease of manufacturing the instant dsRNA agents of the invention.

In certain embodiments of the present invention, an anti-EGFR DsiRNA agent has one or more of the following properties: (i) the DsiRNA agent is asymmetric, *e.g.*, has a 3' overhang on the antisense strand and (ii) the DsiRNA agent has a modified 3' end on the sense strand to direct orientation of Dicer binding and processing of the dsRNA to an active siRNA. According to this embodiment, the longest strand in the dsRNA comprises 25-35 nucleotides (*e.g.*, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34 or 35 nucleotides). In certain such embodiments, the DsiRNA agent is asymmetric such that the sense strand comprises 25-34 nucleotides and the 3' end of the sense strand forms a blunt end with the 5' end of the antisense strand while the antisense strand comprises 26-35 nucleotides and forms an overhang on the 3' end of the antisense strand. In one embodiment, the DsiRNA agent is asymmetric such that the sense strand comprises 25-28 nucleotides and the antisense strand comprises 25-30 nucleotides. Thus, the resulting dsRNA has an overhang on the 3' end of the antisense strand. The overhang is 1-4 nucleotides, for example 2 nucleotides. The sense strand may also have a 5' phosphate.

The DsiRNA agent can also have one or more of the following additional properties: (a) the antisense strand has a right shift from the typical 21mer (*e.g.*, the DsiRNA comprises a length of antisense strand nucleotides that extends to the 5' of a projected Dicer cleavage site within the DsiRNA, with such antisense strand nucleotides base paired with corresponding nucleotides of the sense strand extending 3' of a projected Dicer cleavage site in the sense strand), (b) the strands may not be completely complementary, *i.e.*, the strands may contain simple mismatched base pairs (in certain embodiments, the DsiRNAs of the invention possess 1, 2, 3, 4 or even 5 or more mismatched base pairs, provided that EGFR inhibitory activity of the DsiRNA possessing mismatched base pairs is retained at sufficient levels (*e.g.*, retains at least 50% EGFR inhibitory activity or more, at least 60% EGFR inhibitory activity or more, at least 70% EGFR inhibitory activity or more, at least 80% EGFR inhibitory activity or more, at least 90% EGFR inhibitory activity or more or at least 95% EGFR inhibitory activity or more as compared to a corresponding DsiRNA not possessing mismatched base pairs. In certain embodiments, mismatched base pairs exist between the antisense and sense strands of a DsiRNA. In some embodiments, mismatched base pairs exist (or are predicted to exist) between the antisense strand and the target RNA. In certain

embodiments, the presence of a mismatched base pair(s) between an antisense strand residue and a corresponding residue within the target RNA that is located 3' in the target RNA sequence of a projected Ago2 cleavage site retains and may even enhance EGFR inhibitory activity of a DsiRNA of the invention) and (c) base modifications such as locked nucleic acid(s) may be included in the 5' end of the sense strand. A "typical" 21mer siRNA is designed using conventional techniques. In one technique, a variety of sites are commonly tested in parallel or pools containing several distinct siRNA duplexes specific to the same target with the hope that one of the reagents will be effective (Ji *et al.*, 2003, *FEBS Lett* 552: 247-252). Other techniques use design rules and algorithms to increase the likelihood of obtaining active RNAi effector molecules (Schwarz *et al.*, 2003, *Cell* 115: 199-208; Khvorova *et al.*, 2003, *Cell* 115: 209-216; Ui-Tei *et al.*, 2004, *Nucleic Acids Res* 32: 936-948; Reynolds *et al.*, 2004, *Nat Biotechnol* 22: 326-330; Krol *et al.*, 2004, *J Biol Chem* 279: 42230-42239; Yuan *et al.*, 2004, *Nucl Acids Res* 32(Webserver issue):W130-134; Boese *et al.*, 2005, *Methods Enzymol* 392: 73-96). High throughput selection of siRNA has also been developed (U.S. published patent application No. 2005/0042641 A1). Potential target sites can also be analyzed by secondary structure predictions (Heale *et al.*, 2005, *Nucleic Acids Res* 33(3): e30). This 21mer is then used to design a right shift to include 3-9 additional nucleotides on the 5' end of the 21mer. The sequence of these additional nucleotides is not restricted. In one embodiment, the added ribonucleotides are based on the sequence of the target gene. Even in this embodiment, full complementarity between the target sequence and the antisense siRNA is not required.

The first and second oligonucleotides of a DsiRNA agent of the instant invention are not required to be completely complementary. They only need to be sufficiently complementary to anneal under biological conditions and to provide a substrate for Dicer that produces a siRNA sufficiently complementary to the target sequence. Locked nucleic acids, or LNA's, are well known to a skilled artisan (Elmen *et al.*, 2005, *Nucleic Acids Res* 33: 439-447; Kurreck *et al.*, 2002, *Nucleic Acids Res* 30: 1911-1918; Crinelli *et al.*, 2002, *Nucleic Acids Res* 30: 2435-2443; Braasch and Corey, 2001, *Chem Biol* 8: 1-7; Bondensgaard *et al.*, 2000, *Chemistry* 6: 2687-2695; Wahlestedt *et al.*, 2000, *Proc Natl Acad Sci USA* 97: 5633-5638). In one embodiment, an LNA is incorporated at the 5' terminus of the sense strand. In another embodiment, an LNA is incorporated at the 5' terminus of the sense strand in duplexes designed to include a 3' overhang on the antisense strand.

In certain embodiments, the DsiRNA agent of the instant invention has an asymmetric

structure, with the sense strand having a 25-base pair length, and the antisense strand having a 27-base pair length with a 2 base 3'-overhang. In other embodiments, this DsiRNA agent having an asymmetric structure further contains 2 deoxynucleotides at the 3' end of the sense strand in place of two of the ribonucleotides.

Certain DsiRNA agent compositions containing two separate oligonucleotides can be linked by a third structure. The third structure will not block Dicer activity on the DsiRNA agent and will not interfere with the directed destruction of the RNA transcribed from the target gene. In one embodiment, the third structure may be a chemical linking group. Many suitable chemical linking groups are known in the art and can be used. Alternatively, the third structure may be an oligonucleotide that links the two oligonucleotides of the DsiRNA agent in a manner such that a hairpin structure is produced upon annealing of the two oligonucleotides making up the dsRNA composition. The hairpin structure will not block Dicer activity on the DsiRNA agent and will not interfere with the directed destruction of the EGFR RNA.

EGFR cDNA and Polypeptide Sequences

Known human and mouse EGFR cDNA and polypeptide sequences include the following: human wild-type Epidermal Growth Factor Receptor, transcript variant 1 (EGFR) cDNA sequences GenBank Accession No. NM_005228.3; corresponding human EGFR polypeptide sequence GenBank Accession No. NP_005219.2; mouse wild-type EGFR sequence GenBank Accession No. NM_207655.2 (Mus musculus C57BL/6 EGFR transcript) and corresponding mouse EGFR polypeptide sequence GenBank Accession No. NP_997538.1.

EGFR Cell Biology and Clinical Therapeutics

EGFR (epidermal growth factor receptor) exists on the cell surface and is activated by binding of its specific ligands, including epidermal growth factor and transforming growth factor α (TGF α). ErbB2 has no known direct activating ligand, and may be in an activated state constitutively or become active upon heterodimerization with other family members such as EGFR. Upon activation by its growth factor ligands, EGFR undergoes a transition from an inactive monomeric form to an active homodimer - although there is some evidence that preformed inactive dimers may also exist before ligand binding. In addition to forming

homodimers after ligand binding, EGFR may pair with another member of the ErbB receptor family, such as ErbB2/Her2/neu, to create an activated heterodimer. There is also evidence to suggest that clusters of activated EGFRs form, although it remains unclear whether this clustering is important for activation itself or occurs subsequent to activation of individual dimers.

EGFR dimerization stimulates its intrinsic intracellular protein-tyrosine kinase activity. As a result, autophosphorylation of several tyrosine (Y) residues in the C-terminal domain of EGFR occurs. These include Y992, Y1045, Y1068, Y1148 and Y1173 (Downward *et al. Nature* 311: 483–5). This autophosphorylation elicits downstream activation and signaling by several other proteins that associate with the phosphorylated tyrosines through their own phosphotyrosine-binding SH2 domains. These downstream signaling proteins initiate several signal transduction cascades, principally the MAPK, Akt and JNK pathways, leading to DNA synthesis and cell proliferation (Oda *et al. Mol. Syst. Biol.* 1: 2005). Such proteins modulate phenotypes such as cell migration, adhesion, and proliferation. Activation of the receptor is also important for the innate immune response in human skin (Sorensen *et al. J Clin Invest.* 116: 1878–1885). The kinase domain of EGFR can also cross-phosphorylate tyrosine residues of other receptors it is aggregated with, and can itself be activated in that manner.

Mutations that lead to EGFR overexpression (known as upregulation) or overactivity have been associated with a number of cancers, including lung cancer, anal cancers (Walker *et al. Human Pathology* 40: 1517–1527) and glioblastoma multiforme. In this latter case, a more or less specific mutation of EGFR, called EGFRvIII, is often observed (Kuan *et al. Endocr. Relat. Cancer* 8: 83–96). Mutations, amplifications or misregulations of EGFR or family members are implicated in about 30% of all epithelial cancers.

Mutations involving EGFR can produce constant activation, which can result in uncontrolled cell division – a predisposition for cancer (Lynch *et al. N. Engl. J. Med.* 350: 2129–39). Consequently, mutations of EGFR have been identified in several types of cancer, and it is the target of an expanding class of anticancer therapies (Zhang *et al. J. Clin. Invest.* 117: 2051–8), including, e.g., the molecules disclosed herein.

The identification of EGFR as an oncogene has led to the development of anticancer therapeutics directed against EGFR, including gefitinib (Paez *et al. Science* 304: 1497–500) and erlotinib for lung cancer, and cetuximab for colon cancer.

Many therapeutic approaches target EGFR. Cetuximab and panitumumab are examples of monoclonal antibody inhibitors. However, the former is of the IgG1 type, the latter of the IgG2 type; consequences on antibody-dependent cellular cytotoxicity can be quite different, depending on type of antibody administered (Yan and Beckman. *BioTechniques* 39: 565–8). Other monoclonals in clinical development are zalutumumab, nimotuzumab, and matuzumab. The above-referenced monoclonal antibodies block the extracellular ligand binding domain. With the binding site blocked, signal molecules can no longer attach there and activate the tyrosine kinase.

Another method is using small molecules to inhibit the EGFR tyrosine kinase, which is on the cytoplasmic side of the receptor. Without kinase activity, EGFR is unable to activate itself, which is a prerequisite for binding of downstream adaptor proteins. Ostensibly by halting the signaling cascade in cells that rely on this pathway for growth, tumor proliferation and migration is diminished. Gefitinib, erlotinib, and lapatinib (mixed EGFR and ERBB2 inhibitor) are examples of small molecule kinase inhibitors.

There are several quantitative methods available that use protein phosphorylation detection to identify EGFR family inhibitors (Olive DM. *Expert Rev Proteomics* 1: 327–41).

In recent clinical trials of EGFR-targeting therapeutics, subjects have been divided into EGFR positive and negative, based upon whether a tissue test shows a mutation. In such trials, EGFR positive patients have shown an impressive 60% response rate which exceeds the response rate for conventional chemotherapy (Jackman *et al. Clin. Cancer Res.* 15: 5267–73). However, many patients develop resistance to antibody and/or small molecule therapeutics. Two primary sources of resistance are the T790M Mutation and MET oncogene (Jackman *et al. Clin. Cancer Res.* 15: 5267–73). To date, there exists no consensus of an accepted approach to combat resistance, nor FDA approval of a specific combination.

***In Vitro* Assay to Assess dsRNA EGFR Inhibitory Activity**

An *in vitro* assay that recapitulates RNAi in a cell-free system can be used to evaluate dsRNA constructs targeting EGFR RNA sequence(s), and thus to assess EGFR-specific gene inhibitory activity (also referred to herein as EGFR inhibitory activity) of a dsRNA. The assay comprises the system described by Tuschl *et al.*, 1999, *Genes and Development*, 13, 3191-3197 and Zamore *et al.*, 2000, *Cell*, 101, 25-33 adapted for use with dsRNA (e.g., DsiRNA) agents directed against EGFR RNA. A *Drosophila* extract derived from syncytial blastoderm is used to reconstitute RNAi activity *in vitro*. Target RNA is generated *via in*

in vitro transcription from a selected EGFR expressing plasmid using T7 RNA polymerase or *via* chemical synthesis. Sense and antisense dsRNA strands (for example, 20 uM each) are annealed by incubation in buffer (such as 100 mM potassium acetate, 30 mM HEPES-KOH, pH 7.4, 2 mM magnesium acetate) for 1 minute at 90°C followed by 1 hour at 37°C, then diluted in lysis buffer (for example 100 mM potassium acetate, 30 mM HEPES-KOH at pH 7.4, 2 mM magnesium acetate). Annealing can be monitored by gel electrophoresis on an agarose gel in TBE buffer and stained with ethidium bromide. The *Drosophila* lysate is prepared using zero to two-hour-old embryos from Oregon R flies collected on yeasted molasses agar that are dechorionated and lysed. The lysate is centrifuged and the supernatant isolated. The assay comprises a reaction mixture containing 50% lysate [vol/vol], RNA (10-50 pM final concentration), and 10% [vol/vol] lysis buffer containing dsRNA (10 nM final concentration). The reaction mixture also contains 10 mM creatine phosphate, 10 ug/ml creatine phosphokinase, 100 uM GTP, 100 uM UTP, 100 uM CTP, 500 uM ATP, 5 mM DTT, 0.1 U/uL RNasin (Promega), and 100 uM of each amino acid. The final concentration of potassium acetate is adjusted to 100 mM. The reactions are pre-assembled on ice and preincubated at 25°C for 10 minutes before adding RNA, then incubated at 25°C for an additional 60 minutes. Reactions are quenched with 4 volumes of 1.25xPassive Lysis Buffer (Promega). Target RNA cleavage is assayed by RT-PCR analysis or other methods known in the art and are compared to control reactions in which dsRNA is omitted from the reaction.

Alternately, internally-labeled target RNA for the assay is prepared by *in vitro* transcription in the presence of [α -³²P] CTP, passed over a G50 Sephadex column by spin chromatography and used as target RNA without further purification. Optionally, target RNA is 5'-³²P-end labeled using T4 polynucleotide kinase enzyme. Assays are performed as described above and target RNA and the specific RNA cleavage products generated by RNAi are visualized on an autoradiograph of a gel. The percentage of cleavage is determined by PHOSPHOR IMAGER® (autoradiography) quantitation of bands representing intact control RNA or RNA from control reactions without dsRNA and the cleavage products generated by the assay.

In one embodiment, this assay is used to determine target sites in the EGFR RNA target for dsRNA mediated RNAi cleavage, wherein a plurality of dsRNA constructs are screened for RNAi mediated cleavage of the EGFR RNA target, for example, by analyzing the assay reaction by electrophoresis of labeled target RNA, or by northern blotting, as well as by other methodology well known in the art.

In certain embodiments, a dsRNA of the invention is deemed to possess EGFR inhibitory activity if, *e.g.*, a 50% reduction in EGFR RNA levels is observed in a system, cell, tissue or organism, relative to a suitable control. Additional metes and bounds for determination of EGFR inhibitory activity of a dsRNA of the invention are described *supra*.

Conjugation and Delivery of Anti-EGFR dsRNA Agents

In certain embodiments the present invention relates to a method for treating a subject having an EGFR-associated disease or disorder, or at risk of developing an EGFR-associated disease or disorder. In such embodiments, the dsRNA can act as novel therapeutic agents for controlling the EGFR-associated disease or disorder. The method comprises administering a pharmaceutical composition of the invention to the patient (*e.g.*, human), such that the expression, level and/or activity of an EGFR RNA is reduced. The expression, level and/or activity of a polypeptide encoded by an EGFR RNA might also be reduced by a dsRNA of the instant invention, even where said dsRNA is directed against a non-coding region of the EGFR transcript (*e.g.*, a targeted 5' UTR or 3' UTR sequence). Because of their high specificity, the dsRNAs of the present invention can specifically target EGFR sequences of cells and tissues, optionally in an allele-specific manner where polymorphic alleles exist within an individual and/or population.

In the treatment of an EGFR-associated disease or disorder, the dsRNA can be brought into contact with the cells or tissue of a subject, *e.g.*, the cells or tissue of a subject exhibiting dysregulation of EGFR and/or otherwise targeted for reduction of EGFR levels. For example, dsRNA substantially identical to all or part of an EGFR RNA sequence, may be brought into contact with or introduced into such a cell, either *in vivo* or *in vitro*. Similarly, dsRNA substantially identical to all or part of an EGFR RNA sequence may administered directly to a subject having or at risk of developing an EGFR-associated disease or disorder.

Therapeutic use of the dsRNA agents of the instant invention can involve use of formulations of dsRNA agents comprising multiple different dsRNA agent sequences. For example, two or more, three or more, four or more, five or more, etc. of the presently described agents can be combined to produce a formulation that, *e.g.*, targets multiple different regions of the EGFR RNA, or that not only target EGFR RNA but also target, *e.g.*, cellular target genes associated with an EGFR-associated disease or disorder. A dsRNA agent of the instant invention may also be constructed such that either strand of the dsRNA

agent independently targets two or more regions of EGFR RNA, or such that one of the strands of the dsRNA agent targets a cellular target gene of EGFR known in the art.

Use of multifunctional dsRNA molecules that target more than one region of a target nucleic acid molecule can also provide potent inhibition of EGFR RNA levels and expression. For example, a single multifunctional dsRNA construct of the invention can target both the EGFR-1385 and EGFR-4012 sites simultaneously; additionally and/or alternatively, single or multifunctional agents of the invention can be designed to selectively target one splice variant of EGFR over another.

Thus, the dsRNA agents of the instant invention, individually, or in combination or in conjunction with other drugs, can be used to treat, inhibit, reduce, or prevent an EGFR-associated disease or disorder. For example, the dsRNA molecules can be administered to a subject or can be administered to other appropriate cells evident to those skilled in the art, individually or in combination with one or more drugs under conditions suitable for the treatment.

The dsRNA molecules also can be used in combination with other known treatments to treat, inhibit, reduce, or prevent an EGFR-associated disease or disorder in a subject or organism. For example, the described molecules could be used in combination with one or more known compounds, treatments, or procedures to treat, inhibit, reduce, or prevent an EGFR-associated disease or disorder in a subject or organism as are known in the art.

A dsRNA agent of the invention can be conjugated (*e.g.*, at its 5' or 3' terminus of its sense or antisense strand) or unconjugated to another moiety (*e.g.* a non-nucleic acid moiety such as a peptide), an organic compound (*e.g.*, a dye, cholesterol, or the like). Modifying dsRNA agents in this way may improve cellular uptake or enhance cellular targeting activities of the resulting dsRNA agent derivative as compared to the corresponding unconjugated dsRNA agent, are useful for tracing the dsRNA agent derivative in the cell, or improve the stability of the dsRNA agent derivative compared to the corresponding unconjugated dsRNA agent.

Methods of Introducing Nucleic Acids, Vectors, and Host Cells

dsRNA agents of the invention may be directly introduced into a cell (*i.e.*, intracellularly); or introduced extracellularly into a cavity, interstitial space, into the circulation of an organism, introduced orally, or may be introduced by bathing a cell or organism in a solution containing the nucleic acid. Vascular or extravascular circulation, the

blood or lymph system, and the cerebrospinal fluid are sites where the nucleic acid may be introduced.

The dsRNA agents of the invention can be introduced using nucleic acid delivery methods known in art including injection of a solution containing the nucleic acid, bombardment by particles covered by the nucleic acid, soaking the cell or organism in a solution of the nucleic acid, or electroporation of cell membranes in the presence of the nucleic acid. Other methods known in the art for introducing nucleic acids to cells may be used, such as lipid-mediated carrier transport, chemical-mediated transport, and cationic liposome transfection such as calcium phosphate, and the like. The nucleic acid may be introduced along with other components that perform one or more of the following activities: enhance nucleic acid uptake by the cell or other-wise increase inhibition of the target EGFR RNA.

A cell having a target EGFR RNA may be from the germ line or somatic, totipotent or pluripotent, dividing or non-dividing, parenchyma or epithelium, immortalized or transformed, or the like. The cell may be a stem cell or a differentiated cell. Cell types that are differentiated include adipocytes, fibroblasts, myocytes, cardiomyocytes, endothelium, neurons, glia, blood cells, megakaryocytes, lymphocytes, macrophages, neutrophils, eosinophils, basophils, mast cells, leukocytes, granulocytes, keratinocytes, chondrocytes, osteoblasts, osteoclasts, hepatocytes, and cells of the endocrine or exocrine glands.

Depending on the particular target EGFR RNA sequence and the dose of dsRNA agent material delivered, this process may provide partial or complete loss of function for the EGFR RNA. A reduction or loss of RNA levels or expression (either EGFR RNA expression or encoded polypeptide expression) in at least 50%, 60%, 70%, 80%, 90%, 95% or 99% or more of targeted cells is exemplary. Inhibition of EGFR RNA levels or expression refers to the absence (or observable decrease) in the level of EGFR RNA or EGFR RNA-encoded protein. Specificity refers to the ability to inhibit the EGFR RNA without manifest effects on other genes of the cell. The consequences of inhibition can be confirmed by examination of the outward properties of the cell or organism or by biochemical techniques such as RNA solution hybridization, nuclease protection, Northern hybridization, reverse transcription, gene expression monitoring with a microarray, antibody binding, enzyme linked immunosorbent assay (ELISA), Western blotting, radioimmunoassay (RIA), other immunoassays, and fluorescence activated cell analysis (FACS). Inhibition of target EGFR RNA sequence(s) by the dsRNA agents of the invention also can be measured based upon the

effect of administration of such dsRNA agents upon development/progression of an EGFR-associated disease or disorder, *e.g.*, tumor formation, growth, metastasis, etc., either *in vivo* or *in vitro*. Treatment and/or reductions in tumor or cancer cell levels can include halting or reduction of growth of tumor or cancer cell levels or reductions of, *e.g.*, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95% or 99% or more, and can also be measured in logarithmic terms, *e.g.*, 10-fold, 100-fold, 1000-fold, 10^5 -fold, 10^6 -fold, 10^7 -fold reduction in cancer cell levels could be achieved *via* administration of the dsRNA agents of the invention to cells, a tissue, or a subject.

For RNA-mediated inhibition in a cell line or whole organism, expression a reporter or drug resistance gene whose protein product is easily assayed can be measured. Such reporter genes include acetohydroxyacid synthase (AHAS), alkaline phosphatase (AP), beta galactosidase (LacZ), beta glucuronidase (GUS), chloramphenicol acetyltransferase (CAT), green fluorescent protein (GFP), horseradish peroxidase (HRP), luciferase (Luc), nopaline synthase (NOS), octopine synthase (OCS), and derivatives thereof. Multiple selectable markers are available that confer resistance to ampicillin, bleomycin, chloramphenicol, gentamycin, hygromycin, kanamycin, lincomycin, methotrexate, phosphinothricin, puromycin, and tetracyclin. Depending on the assay, quantitation of the amount of gene expression allows one to determine a degree of inhibition which is greater than 10%, 33%, 50%, 90%, 95% or 99% as compared to a cell not treated according to the present invention.

Lower doses of injected material and longer times after administration of RNA silencing agent may result in inhibition in a smaller fraction of cells (*e.g.*, at least 10%, 20%, 50%, 75%, 90%, or 95% of targeted cells). Quantitation of gene expression in a cell may show similar amounts of inhibition at the level of accumulation of target EGFR RNA or translation of target protein. As an example, the efficiency of inhibition may be determined by assessing the amount of gene product in the cell; RNA may be detected with a hybridization probe having a nucleotide sequence outside the region used for the inhibitory dsRNA, or translated polypeptide may be detected with an antibody raised against the polypeptide sequence of that region.

The dsRNA agent may be introduced in an amount which allows delivery of at least one copy per cell. Higher doses (*e.g.*, at least 5, 10, 100, 500 or 1000 copies per cell) of material may yield more effective inhibition; lower doses may also be useful for specific applications.

Pharmaceutical Compositions

In certain embodiments, the present invention provides for a pharmaceutical composition comprising the dsRNA agent of the present invention. The dsRNA agent sample can be suitably formulated and introduced into the environment of the cell by any means that allows for a sufficient portion of the sample to enter the cell to induce gene silencing, if it is to occur. Many formulations for dsRNA are known in the art and can be used so long as the dsRNA gains entry to the target cells so that it can act. *See, e.g.*, U.S. published patent application Nos. 2004/0203145 A1 and 2005/0054598 A1. For example, the dsRNA agent of the instant invention can be formulated in buffer solutions such as phosphate buffered saline solutions, liposomes, micellar structures, and capsids. Formulations of dsRNA agent with cationic lipids can be used to facilitate transfection of the dsRNA agent into cells. For example, cationic lipids, such as lipofectin (U.S. Pat. No. 5,705,188), cationic glycerol derivatives, and polycationic molecules, such as polylysine (published PCT International Application WO 97/30731), can be used. Suitable lipids include Oligofectamine, Lipofectamine (Life Technologies), NC388 (Ribozyme Pharmaceuticals, Inc., Boulder, Colo.), or FuGene 6 (Roche) all of which can be used according to the manufacturer's instructions.

Such compositions typically include the nucleic acid molecule and a pharmaceutically acceptable carrier. As used herein the language "pharmaceutically acceptable carrier" includes saline, solvents, dispersion media, coatings, antibacterial and antifungal agents, isotonic and absorption delaying agents, and the like, compatible with pharmaceutical administration. Supplementary active compounds can also be incorporated into the compositions.

A pharmaceutical composition is formulated to be compatible with its intended route of administration. Examples of routes of administration include parenteral, e.g., intravenous, intradermal, subcutaneous, oral (e.g., inhalation), transdermal (topical), transmucosal, and rectal administration. Solutions or suspensions used for parenteral, intradermal, or subcutaneous application can include the following components: a sterile diluent such as water for injection, saline solution, fixed oils, polyethylene glycols, glycerine, propylene glycol or other synthetic solvents; antibacterial agents such as benzyl alcohol or methyl parabens; antioxidants such as ascorbic acid or sodium bisulfite; chelating agents such as ethylenediaminetetraacetic acid; buffers such as acetates, citrates or phosphates and agents

for the adjustment of tonicity such as sodium chloride or dextrose. pH can be adjusted with acids or bases, such as hydrochloric acid or sodium hydroxide. The parenteral preparation can be enclosed in ampoules, disposable syringes or multiple dose vials made of glass or plastic.

Pharmaceutical compositions suitable for injectable use include sterile aqueous solutions (where water soluble) or dispersions and sterile powders for the extemporaneous preparation of sterile injectable solutions or dispersion. For intravenous administration, suitable carriers include physiological saline, bacteriostatic water, Cremophor EL.TM. (BASF, Parsippany, N.J.) or phosphate buffered saline (PBS). In all cases, the composition must be sterile and should be fluid to the extent that easy syringability exists. It should be stable under the conditions of manufacture and storage and must be preserved against the contaminating action of microorganisms such as bacteria and fungi. The carrier can be a solvent or dispersion medium containing, for example, water, ethanol, polyol (for example, glycerol, propylene glycol, and liquid polyethethylene glycol, and the like), and suitable mixtures thereof. The proper fluidity can be maintained, for example, by the use of a coating such as lecithin, by the maintenance of the required particle size in the case of dispersion and by the use of surfactants. Prevention of the action of microorganisms can be achieved by various antibacterial and antifungal agents, for example, parabens, chlorobutanol, phenol, ascorbic acid, thimerosal, and the like. In many cases, it will be preferable to include isotonic agents, for example, sugars, polyalcohols such as manitol, sorbitol, sodium chloride in the composition. Prolonged absorption of the injectable compositions can be brought about by including in the composition an agent which delays absorption, for example, aluminum monostearate and gelatin.

Sterile injectable solutions can be prepared by incorporating the active compound in the required amount in a selected solvent with one or a combination of ingredients enumerated above, as required, followed by filtered sterilization. Generally, dispersions are prepared by incorporating the active compound into a sterile vehicle, which contains a basic dispersion medium and the required other ingredients from those enumerated above. In the case of sterile powders for the preparation of sterile injectable solutions, the preferred methods of preparation are vacuum drying and freeze-drying which yields a powder of the active ingredient plus any additional desired ingredient from a previously sterile-filtered solution thereof.

Oral compositions generally include an inert diluent or an edible carrier. For the

purpose of oral therapeutic administration, the active compound can be incorporated with excipients and used in the form of tablets, troches, or capsules, e.g., gelatin capsules. Oral compositions can also be prepared using a fluid carrier for use as a mouthwash.

Pharmaceutically compatible binding agents, and/or adjuvant materials can be included as part of the composition. The tablets, pills, capsules, troches and the like can contain any of the following ingredients, or compounds of a similar nature: a binder such as microcrystalline cellulose, gum tragacanth or gelatin; an excipient such as starch or lactose, a disintegrating agent such as alginic acid, Primogel, or corn starch; a lubricant such as magnesium stearate or Sterotes; a glidant such as colloidal silicon dioxide; a sweetening agent such as sucrose or saccharin; or a flavoring agent such as peppermint, methyl salicylate, or orange flavoring.

For administration by inhalation, the compounds are delivered in the form of an aerosol spray from pressured container or dispenser which contains a suitable propellant, e.g., a gas such as carbon dioxide, or a nebulizer. Such methods include those described in U.S. Pat. No. 6,468,798.

Systemic administration can also be by transmucosal or transdermal means. For transmucosal or transdermal administration, penetrants appropriate to the barrier to be permeated are used in the formulation. Such penetrants are generally known in the art, and include, for example, for transmucosal administration, detergents, bile salts, and fusidic acid derivatives. Transmucosal administration can be accomplished through the use of nasal sprays or suppositories. For transdermal administration, the active compounds are formulated into ointments, salves, gels, or creams as generally known in the art.

The compounds can also be prepared in the form of suppositories (e.g., with conventional suppository bases such as cocoa butter and other glycerides) or retention enemas for rectal delivery.

The compounds can also be administered by transfection or infection using methods known in the art, including but not limited to the methods described in McCaffrey et al. (2002), *Nature*, 418(6893), 38-9 (hydrodynamic transfection); Xia et al. (2002), *Nature Biotechnol.*, 20(10), 1006-10 (viral-mediated delivery); or Putnam (1996), *Am. J. Health Syst. Pharm.* 53(2), 151-160, erratum at *Am. J. Health Syst. Pharm.* 53(3), 325 (1996).

The compounds can also be administered by a method suitable for administration of nucleic acid agents, such as a DNA vaccine. These methods include gene guns, bio injectors, and skin patches as well as needle-free methods such as the micro-particle DNA vaccine technology disclosed in U.S. Pat. No. 6,194,389, and the mammalian transdermal needle-free

vaccination with powder-form vaccine as disclosed in U.S. Pat. No. 6,168,587. Additionally, intranasal delivery is possible, as described in, inter alia, Hamajima et al. (1998), Clin. Immunol. Immunopathol., 88(2), 205-10. Liposomes (e.g., as described in U.S. Pat. No. 6,472,375) and microencapsulation can also be used. Biodegradable targetable microparticle delivery systems can also be used (e.g., as described in U.S. Pat. No. 6,471,996).

In one embodiment, the active compounds are prepared with carriers that will protect the compound against rapid elimination from the body, such as a controlled release formulation, including implants and microencapsulated delivery systems. Biodegradable, biocompatible polymers can be used, such as ethylene vinyl acetate, polyanhydrides, polyglycolic acid, collagen, polyorthoesters, and polylactic acid. Such formulations can be prepared using standard techniques. The materials can also be obtained commercially from Alza Corporation and Nova Pharmaceuticals, Inc. Liposomal suspensions (including liposomes targeted to infected cells with monoclonal antibodies to viral antigens) can also be used as pharmaceutically acceptable carriers. These can be prepared according to methods known to those skilled in the art, for example, as described in U.S. Patent No. 4,522,811.

Toxicity and therapeutic efficacy of such compounds can be determined by standard pharmaceutical procedures in cell cultures or experimental animals, e.g., for determining the LD₅₀ (the dose lethal to 50% of the population) and the ED₅₀ (the dose therapeutically effective in 50% of the population). The dose ratio between toxic and therapeutic effects is the therapeutic index and it can be expressed as the ratio LD₅₀/ED₅₀. Compounds which exhibit high therapeutic indices are preferred. While compounds that exhibit toxic side effects may be used, care should be taken to design a delivery system that targets such compounds to the site of affected tissue in order to minimize potential damage to uninfected cells and, thereby, reduce side effects.

The data obtained from the cell culture assays and animal studies can be used in formulating a range of dosage for use in humans. The dosage of such compounds lies preferably within a range of circulating concentrations that include the ED₅₀ with little or no toxicity. The dosage may vary within this range depending upon the dosage form employed and the route of administration utilized. For a compound used in the method of the invention, the therapeutically effective dose can be estimated initially from cell culture assays. A dose may be formulated in animal models to achieve a circulating plasma concentration range that includes the IC₅₀ (*i.e.*, the concentration of the test compound which achieves a half-maximal inhibition of symptoms) as determined in cell culture. Such information can be used to more

accurately determine useful doses in humans. Levels in plasma may be measured, for example, by high performance liquid chromatography.

As defined herein, a therapeutically effective amount of a nucleic acid molecule (i.e., an effective dosage) depends on the nucleic acid selected. For instance, single dose amounts of a dsRNA (or, *e.g.*, a construct(s) encoding for such dsRNA) in the range of approximately 1 pg to 1000 mg may be administered; in some embodiments, 10, 30, 100, or 1000 pg, or 10, 30, 100, or 1000 ng, or 10, 30, 100, or 1000 µg, or 10, 30, 100, or 1000 mg may be administered. In some embodiments, 1-5 g of the compositions can be administered. The compositions can be administered one from one or more times per day to one or more times per week; including once every other day. The skilled artisan will appreciate that certain factors may influence the dosage and timing required to effectively treat a subject, including but not limited to the severity of the disease or disorder, previous treatments, the general health and/or age of the subject, and other diseases present. Moreover, treatment of a subject with a therapeutically effective amount of a nucleic acid (*e.g.*, dsRNA), protein, polypeptide, or antibody can include a single treatment or, preferably, can include a series of treatments.

The nucleic acid molecules of the invention can be inserted into expression constructs, *e.g.*, viral vectors, retroviral vectors, expression cassettes, or plasmid viral vectors, *e.g.*, using methods known in the art, including but not limited to those described in Xia et al., (2002), *supra*. Expression constructs can be delivered to a subject by, for example, inhalation, orally, intravenous injection, local administration (see U.S. Pat. No. 5,328,470) or by stereotactic injection (see *e.g.*, Chen et al. (1994), *Proc. Natl. Acad. Sci. USA*, 91, 3054-3057). The pharmaceutical preparation of the delivery vector can include the vector in an acceptable diluent, or can comprise a slow release matrix in which the delivery vehicle is imbedded. Alternatively, where the complete delivery vector can be produced intact from recombinant cells, *e.g.*, retroviral vectors, the pharmaceutical preparation can include one or more cells which produce the gene delivery system.

The expression constructs may be constructs suitable for use in the appropriate expression system and include, but are not limited to retroviral vectors, linear expression cassettes, plasmids and viral or virally-derived vectors, as known in the art. Such expression constructs may include one or more inducible promoters, RNA Pol III promoter systems such as U6 snRNA promoters or H1 RNA polymerase III promoters, or other promoters known in the art. The constructs can include one or both strands of the siRNA. Expression constructs expressing both strands can also include loop structures linking both strands, or each strand

can be separately transcribed from separate promoters within the same construct. Each strand can also be transcribed from a separate expression construct, *e.g.*, Tuschl (2002, *Nature Biotechnol* 20: 500-505).

It can be appreciated that the method of introducing dsRNA agents into the environment of the cell will depend on the type of cell and the make up of its environment. For example, when the cells are found within a liquid, one preferable formulation is with a lipid formulation such as in lipofectamine and the dsRNA agents can be added directly to the liquid environment of the cells. Lipid formulations can also be administered to animals such as by intravenous, intramuscular, or intraperitoneal injection, or orally or by inhalation or other methods as are known in the art. When the formulation is suitable for administration into animals such as mammals and more specifically humans, the formulation is also pharmaceutically acceptable. Pharmaceutically acceptable formulations for administering oligonucleotides are known and can be used. In some instances, it may be preferable to formulate dsRNA agents in a buffer or saline solution and directly inject the formulated dsRNA agents into cells, as in studies with oocytes. The direct injection of dsRNA agent duplexes may also be done. For suitable methods of introducing dsRNA (*e.g.*, DsiRNA agents), see U.S. published patent application No. 2004/0203145 A1.

Suitable amounts of a dsRNA agent must be introduced and these amounts can be empirically determined using standard methods. Typically, effective concentrations of individual dsRNA agent species in the environment of a cell will be 50 nanomolar or less, 10 nanomolar or less, or compositions in which concentrations of 1 nanomolar or less can be used. In another embodiment, methods utilizing a concentration of 200 picomolar or less, 100 picomolar or less, 50 picomolar or less, 20 picomolar or less, and even a concentration of 10 picomolar or less, 5 picomolar or less, 2 picomolar or less or 1 picomolar or less can be used in many circumstances.

The method can be carried out by addition of the dsRNA agent compositions to an extracellular matrix in which cells can live provided that the dsRNA agent composition is formulated so that a sufficient amount of the dsRNA agent can enter the cell to exert its effect. For example, the method is amenable for use with cells present in a liquid such as a liquid culture or cell growth media, in tissue explants, or in whole organisms, including animals, such as mammals and especially humans.

The level or activity of an EGFR RNA can be determined by a suitable method now known in the art or that is later developed. It can be appreciated that the method used to

measure a target RNA and/or the expression of a target RNA can depend upon the nature of the target RNA. For example, where the target EGFR RNA sequence encodes a protein, the term "expression" can refer to a protein or the EGFR RNA/transcript derived from the EGFR gene (either genomic or of exogenous origin). In such instances the expression of the target EGFR RNA can be determined by measuring the amount of EGFR RNA/transcript directly or by measuring the amount of EGFR protein. Protein can be measured in protein assays such as by staining or immunoblotting or, if the protein catalyzes a reaction that can be measured, by measuring reaction rates. All such methods are known in the art and can be used. Where target EGFR RNA levels are to be measured, art-recognized methods for detecting RNA levels can be used (*e.g.*, RT-PCR, Northern Blotting, etc.). In targeting EGFR RNAs with the dsRNA agents of the instant invention, it is also anticipated that measurement of the efficacy of a dsRNA agent in reducing levels of EGFR RNA or protein in a subject, tissue, in cells, either *in vitro* or *in vivo*, or in cell extracts can also be used to determine the extent of reduction of EGFR-associated phenotypes (*e.g.*, disease or disorders, *e.g.*, cancer or tumor formation, growth, metastasis, spread, etc.). The above measurements can be made on cells, cell extracts, tissues, tissue extracts or other suitable source material.

The determination of whether the expression of an EGFR RNA has been reduced can be by a suitable method that can reliably detect changes in RNA levels. Typically, the determination is made by introducing into the environment of a cell undigested dsRNA such that at least a portion of that dsRNA agent enters the cytoplasm, and then measuring the level of the target RNA. The same measurement is made on identical untreated cells and the results obtained from each measurement are compared.

The dsRNA agent can be formulated as a pharmaceutical composition which comprises a pharmacologically effective amount of a dsRNA agent and pharmaceutically acceptable carrier. A pharmacologically or therapeutically effective amount refers to that amount of a dsRNA agent effective to produce the intended pharmacological, therapeutic or preventive result. The phrases "pharmacologically effective amount" and "therapeutically effective amount" or simply "effective amount" refer to that amount of an RNA effective to produce the intended pharmacological, therapeutic or preventive result. For example, if a given clinical treatment is considered effective when there is at least a 20% reduction in a measurable parameter associated with a disease or disorder, a therapeutically effective amount of a drug for the treatment of that disease or disorder is the amount necessary to effect at least a 20% reduction in that parameter.

Suitably formulated pharmaceutical compositions of this invention can be administered by means known in the art such as by parenteral routes, including intravenous, intramuscular, intraperitoneal, subcutaneous, transdermal, airway (aerosol), rectal, vaginal and topical (including buccal and sublingual) administration. In some embodiments, the pharmaceutical compositions are administered by intravenous or intraparenteral infusion or injection.

In general, a suitable dosage unit of dsRNA will be in the range of 0.001 to 0.25 milligrams per kilogram body weight of the recipient per day, or in the range of 0.01 to 20 micrograms per kilogram body weight per day, or in the range of 0.001 to 5 micrograms per kilogram of body weight per day, or in the range of 1 to 500 nanograms per kilogram of body weight per day, or in the range of 0.01 to 10 micrograms per kilogram body weight per day, or in the range of 0.10 to 5 micrograms per kilogram body weight per day, or in the range of 0.1 to 2.5 micrograms per kilogram body weight per day. A pharmaceutical composition comprising the dsRNA can be administered once daily. However, the therapeutic agent may also be dosed in dosage units containing two, three, four, five, six or more sub-doses administered at appropriate intervals throughout the day. In that case, the dsRNA contained in each sub-dose must be correspondingly smaller in order to achieve the total daily dosage unit. The dosage unit can also be compounded for a single dose over several days, e.g., using a conventional sustained release formulation which provides sustained and consistent release of the dsRNA over a several day period. Sustained release formulations are well known in the art. In this embodiment, the dosage unit contains a corresponding multiple of the daily dose. Regardless of the formulation, the pharmaceutical composition must contain dsRNA in a quantity sufficient to inhibit expression of the target gene in the animal or human being treated. The composition can be compounded in such a way that the sum of the multiple units of dsRNA together contain a sufficient dose.

Data can be obtained from cell culture assays and animal studies to formulate a suitable dosage range for humans. The dosage of compositions of the invention lies within a range of circulating concentrations that include the ED₅₀ (as determined by known methods) with little or no toxicity. The dosage may vary within this range depending upon the dosage form employed and the route of administration utilized. For a compound used in the method of the invention, the therapeutically effective dose can be estimated initially from cell culture assays. A dose may be formulated in animal models to achieve a circulating plasma concentration range of the compound that includes the IC₅₀ (i.e., the concentration of the test

compound which achieves a half-maximal inhibition of symptoms) as determined in cell culture. Such information can be used to more accurately determine useful doses in humans. Levels of dsRNA in plasma may be measured by standard methods, for example, by high performance liquid chromatography.

The pharmaceutical compositions can be included in a kit, container, pack, or dispenser together with instructions for administration.

Methods of Treatment

The present invention provides for both prophylactic and therapeutic methods of treating a subject at risk of (or susceptible to) a disease or disorder caused, in whole or in part, by EGFR (*e.g.*, misregulation and/or elevation of EGFR transcript and/or EGFR protein levels), or treatable *via* selective targeting of EGFR.

"Treatment", or "treating" as used herein, is defined as the application or administration of a therapeutic agent (*e.g.*, a dsRNA agent or vector or transgene encoding same) to a patient, or application or administration of a therapeutic agent to an isolated tissue or cell line from a patient, who has the disease or disorder, a symptom of disease or disorder or a predisposition toward a disease or disorder, with the purpose to cure, heal, alleviate, relieve, alter, remedy, ameliorate, improve or affect the disease or disorder, the symptoms of the disease or disorder, or the predisposition toward disease.

In one aspect, the invention provides a method for preventing in a subject, a disease or disorder as described above (including, *e.g.*, prevention of the commencement of transforming events within a subject *via* inhibition of EGFR expression), by administering to the subject a therapeutic agent (*e.g.*, a dsRNA agent or vector or transgene encoding same). Subjects at risk for the disease can be identified by, for example, one or a combination of diagnostic or prognostic assays as described herein. Administration of a prophylactic agent can occur prior to the detection of, *e.g.*, cancer in a subject, or the manifestation of symptoms characteristic of the disease or disorder, such that the disease or disorder is prevented or, alternatively, delayed in its progression.

Another aspect of the invention pertains to methods of treating subjects therapeutically, *i.e.*, altering the onset of symptoms of the disease or disorder. These methods can be performed *in vitro* (*e.g.*, by culturing the cell with the dsRNA agent) or, alternatively, *in vivo* (*e.g.*, by administering the dsRNA agent to a subject).

With regards to both prophylactic and therapeutic methods of treatment, such treatments may be specifically tailored or modified, based on knowledge obtained from the field of pharmacogenomics. "Pharmacogenomics", as used herein, refers to the application of genomics technologies such as gene sequencing, statistical genetics, and gene expression analysis to drugs in clinical development and on the market. More specifically, the term refers the study of how a patient's genes determine his or her response to a drug (*e.g.*, a patient's "drug response phenotype", or "drug response genotype"). Thus, another aspect of the invention provides methods for tailoring an individual's prophylactic or therapeutic treatment with either the target EGFR RNA molecules of the present invention or target EGFR RNA modulators according to that individual's drug response genotype. Pharmacogenomics allows a clinician or physician to target prophylactic or therapeutic treatments to patients who will most benefit from the treatment and to avoid treatment of patients who will experience toxic drug-related side effects.

Therapeutic agents can be tested in a selected animal model. For example, a dsRNA agent (or expression vector or transgene encoding same) as described herein can be used in an animal model to determine the efficacy, toxicity, or side effects of treatment with said agent. Alternatively, an agent (*e.g.*, a therapeutic agent) can be used in an animal model to determine the mechanism of action of such an agent.

Models Useful to Evaluate the Down-Regulation of EGFR mRNA Levels and Expression

Cell Culture

The dsRNA agents of the invention can be tested for cleavage activity *in vivo*, for example, using the following procedure. The nucleotide sequences within the EGFR cDNA targeted by the dsRNA agents of the invention are shown in the above EGFR sequences.

The dsRNA reagents of the invention can be tested in cell culture using HeLa or other mammalian cells to determine the extent of EGFR RNA and EGFR protein inhibition. In certain embodiments, DsiRNA reagents (*e.g.*, see Figure 1, and above-recited structures) are selected against the EGFR target as described herein. EGFR RNA inhibition is measured after delivery of these reagents by a suitable transfection agent to, for example, cultured HeLa cells or other transformed or non-transformed mammalian cells in culture. Relative amounts of target EGFR RNA are measured versus actin or other appropriate control using real-time

PCR monitoring of amplification (*e.g.*, ABI 7700 TAQMAN®). A comparison is made to a mixture of oligonucleotide sequences made to unrelated targets or to a randomized DsiRNA control with the same overall length and chemistry, but randomly substituted at each position, or simply to appropriate vehicle-treated or untreated controls. Primary and secondary lead reagents are chosen for the target and optimization performed. After a transfection agent concentration is chosen, a RNA time-course of inhibition is performed with the lead DsiRNA molecule.

TAQMAN® (Real-Time PCR Monitoring of Amplification) and Lightcycler Quantification of mRNA

Total RNA is prepared from cells following DsiRNA delivery, for example, using Ambion Rnaqueous 4-PCR purification kit for large scale extractions, or Promega SV96 for 96-well assays. For Taqman analysis, dual-labeled probes are synthesized with, for example, the reporter dyes FAM or VIC covalently linked at the 5'-end and the quencher dye TAMEGFRA conjugated to the 3'-end. PCR amplifications are performed on, for example, an ABI PRISM 7700 Sequence detector using 50 uL reactions consisting of 10 uL total RNA, 100 nM forward primer, 100 mM reverse primer, 100 nM probe, 1xTaqMan PCR reaction buffer (PE-Applied Biosystems), 5.5 mM MgCl₂, 100 uM each dATP, dCTP, dGTP and dTTP, 0.2U RNase Inhibitor (Promega), 0.025U AmpliTaq Gold (PE-Applied Biosystems) and 0.2U M-MLV Reverse Transcriptase (Promega). The thermal cycling conditions can consist of 30 minutes at 48°C, 10 minutes at 95°C, followed by 40 cycles of 15 seconds at 95°C and 1 minute at 60°C. Quantitation of target EGFR mRNA level is determined relative to standards generated from serially diluted total cellular RNA (300, 100, 30, 10 ng/rxn) and normalizing to, for example, 36B4 mRNA in either parallel or same tube TaqMan reactions.

Western Blotting

Cellular protein extracts can be prepared using a standard micro preparation technique (for example using RIPA buffer), or preferably, by extracting nuclear proteins by a method such as the NE-PER Nuclear and Cytoplasmic Extraction kit (Thermo-Fisher Scientific). Cellular protein extracts are run on 4-12% Tris-Glycine polyacrylamide gel and transferred onto membranes. Non-specific binding can be blocked by incubation, for example, with 5% non-fat milk for 1 hour followed by primary antibody for 16 hours at 4°C. Following washes, the secondary antibody is applied, for example (1:10,000 dilution) for 1 hour at room temperature and the signal detected on a VersaDoc imaging system

In several cell culture systems, cationic lipids have been shown to enhance the bioavailability of oligonucleotides to cells in culture (Bennet, et al., 1992, Mol. Pharmacology, 41, 1023-1033). In one embodiment, dsRNA molecules of the invention are complexed with cationic lipids for cell culture experiments. dsRNA and cationic lipid mixtures are prepared in serum-free OptiMEM (Invitrogen) immediately prior to addition to the cells. OptiMEM is warmed to room temperature (about 20-25°C) and cationic lipid is added to the final desired concentration. dsRNA molecules are added to OptiMEM to the desired concentration and the solution is added to the diluted dsRNA and incubated for 15 minutes at room temperature. In dose response experiments, the RNA complex is serially diluted into OptiMEM prior to addition of the cationic lipid.

Animal Models

The efficacy of anti-EGFR dsRNA agents may be evaluated in an animal model. Animal models of cancer and/or proliferative diseases, conditions, or disorders as are known in the art can be used for evaluation of the efficacy, potency, toxicity, etc. of anti-EGFR dsRNAs. Suitable animal models of proliferative disease include, *e.g.*, transgenic rodents (*e.g.*, mice, rats) bearing gain of function proto-oncogenes (*e.g.*, Myc, Src) and/or loss of function of tumour suppressor proteins (*e.g.*, p53, Rb) or rodents that have been exposed to radiation or chemical mutagens that induce DNA changes that facilitate neoplastic transformation. Many such animal models are commercially available, for example, from The Jackson Laboratory, Bar Harbor, ME, USA. These animal models may be used as a source cells or tissue for assays of the compositions of the invention. Such models can also be used or adapted for use for pre-clinical evaluation of the efficacy of dsRNA compositions of the invention in modulating EGFR gene expression toward therapeutic use.

As in cell culture models, the most EGFR relevant mouse tumor xenografts are those derived from cancer cells that express EGFR proteins. Xenograft mouse models of cancer relevant to study of the anti-tumor effect of modulating EGFR have been described by various groups (*e.g.*, Thomson et al., Cancer Res 2005; 65: 9455; Wakeling et al., Cancer Res 2002; 62: 5749). Use of these models has demonstrated that inhibition of EGFR activity by anti-EGFR agents causes inhibition of tumor growth in animals.

Such models can be used in evaluating the efficacy of dsRNA molecules of the invention to inhibit EGFR activity, expression, tumor/cancer formation, growth, spread, development of other EGFR-associated phenotypes, diseases or disorders, etc. These models

and others can similarly be used to evaluate the safety/toxicity and efficacy of dsRNA molecules of the invention in a pre-clinical setting.

Specific examples of animal model systems useful for evaluation of the EGFR-targeting dsRNAs of the invention include wild-type mice, and orthotopic or subcutaneous tumor model mice, such as those using xenografts of H292, HT29, A431, Du145, or H441 tumor cells. In an exemplary *in vivo* experiment, dsRNAs of the invention are tail vein injected into such mouse models at doses ranging from 1 to 10 mg/kg or, alternatively, repeated doses are administered at single-dose IC₅₀ levels, and organs (*e.g.*, prostate, liver, kidney, lung, pancreas, colon, skin, spleen, bone marrow, lymph nodes, mammary fat pad, etc.) are harvested 24 hours after administration of the final dose. Such organs are then evaluated for mouse and/or human EGFR levels, depending upon the model used. Duration of action can also be examined at, *e.g.*, 1, 4, 7, 14, 21 or more days after final dsRNA administration.

The practice of the present invention employs, unless otherwise indicated, conventional techniques of chemistry, molecular biology, microbiology, recombinant DNA, genetics, immunology, cell biology, cell culture and transgenic biology, which are within the skill of the art. See, *e.g.*, Maniatis et al., 1982, *Molecular Cloning* (Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y.); Sambrook et al., 1989, *Molecular Cloning*, 2nd Ed. (Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y.); Sambrook and Russell, 2001, *Molecular Cloning*, 3rd Ed. (Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y.); Ausubel et al., 1992), *Current Protocols in Molecular Biology* (John Wiley & Sons, including periodic updates); Glover, 1985, *DNA Cloning* (IRL Press, Oxford); Anand, 1992; Guthrie and Fink, 1991; Harlow and Lane, 1988, *Antibodies*, (Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y.); Jakoby and Pastan, 1979; *Nucleic Acid Hybridization* (B. D. Hames & S. J. Higgins eds. 1984); *Transcription And Translation* (B. D. Hames & S. J. Higgins eds. 1984); *Culture Of Animal Cells* (R. I. Freshney, Alan R. Liss, Inc., 1987); *Immobilized Cells And Enzymes* (IRL Press, 1986); B. Perbal, *A Practical Guide To Molecular Cloning* (1984); the treatise, *Methods In Enzymology* (Academic Press, Inc., N.Y.); *Gene Transfer Vectors For Mammalian Cells* (J. H. Miller and M. P. Calos eds., 1987, Cold Spring Harbor Laboratory); *Methods In Enzymology*, Vols. 154 and 155 (Wu et al. eds.), *Immunochemical Methods In Cell And Molecular Biology* (Mayer and Walker, eds., Academic Press, London, 1987); *Handbook Of Experimental Immunology*, Volumes I-IV (D.

M. Weir and C. C. Blackwell, eds., 1986); Riott, *Essential Immunology*, 6th Edition, Blackwell Scientific Publications, Oxford, 1988; Hogan et al., *Manipulating the Mouse Embryo*, (Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y., 1986); Westerfield, M., *The zebrafish book. A guide for the laboratory use of zebrafish (*Danio rerio*)*, (4th Ed., Univ. of Oregon Press, Eugene, 2000).

Unless otherwise defined, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention belongs. Although methods and materials similar or equivalent to those described herein can be used in the practice or testing of the present invention, suitable methods and materials are described below. All publications, patent applications, patents, and other references mentioned herein are incorporated by reference in their entirety. In case of conflict, the present specification, including definitions, will control. In addition, the materials, methods, and examples are illustrative only and not intended to be limiting.

EXAMPLES

The present invention is described by reference to the following Examples, which are offered by way of illustration and are not intended to limit the invention in any manner. Standard techniques well known in the art or the techniques specifically described below were utilized.

Example 1: Preparation of Double-Stranded RNA Oligonucleotides

Oligonucleotide Synthesis and Purification

DsiRNA molecules can be designed to interact with various sites in the RNA message, for example, target sequences within the RNA sequences described herein. In presently exemplified agents, 260 human target EGFR sequences and 96 mouse target EGFR sequences were selected for evaluation (136 of the 260 human target EGFR sites were predicted to be conserved with corresponding sites in the mouse EGFR transcript sequence). The sequences of one strand of the DsiRNA molecules were complementary to the target EGFR site sequences described above. The DsiRNA molecules were chemically synthesized using methods described herein. Generally, DsiRNA constructs were synthesized using solid phase oligonucleotide synthesis methods as described for 19-23mer siRNAs (see for example Usman *et al.*, U.S. Pat. Nos. 5,804,683; 5,831,071; 5,998,203; 6,117,657; 6,353,098;

6,362,323; 6,437,117; 6,469,158; Scaringe *et al.*, U.S. Pat. Nos. 6,111,086; 6,008,400; 6,111,086).

Individual RNA strands were synthesized and HPLC purified according to standard methods (Integrated DNA Technologies, Coralville, Iowa). For example, RNA oligonucleotides were synthesized using solid phase phosphoramidite chemistry, deprotected and desalted on NAP-5 columns (Amersham Pharmacia Biotech, Piscataway, N.J.) using standard techniques (Damha and Olgivie, 1993, *Methods Mol Biol* 20: 81-114; Wincott *et al.*, 1995, *Nucleic Acids Res* 23: 2677-84). The oligomers were purified using ion-exchange high performance liquid chromatography (IE-HPLC) on an Amersham Source 15Q column (1.0 cm x 25 cm; Amersham Pharmacia Biotech, Piscataway, N.J.) using a 15 min step-linear gradient. The gradient varies from 90:10 Buffers A:B to 52:48 Buffers A:B, where Buffer A is 100 mM Tris pH 8.5 and Buffer B is 100 mM Tris pH 8.5, 1 M NaCl. Samples were monitored at 260 nm and peaks corresponding to the full-length oligonucleotide species are collected, pooled, desalted on NAP-5 columns, and lyophilized.

The purity of each oligomer was determined by capillary electrophoresis (CE) on a Beckman PACE 5000 (Beckman Coulter, Inc., Fullerton, Calif.). The CE capillaries had a 100 μ m inner diameter and contains ssDNA 100R Gel (Beckman-Coulter). Typically, about 0.6 nmole of oligonucleotide was injected into a capillary, run in an electric field of 444 V/cm and detected by UV absorbance at 260 nm. Denaturing Tris-Borate-7 M-urea running buffer was purchased from Beckman-Coulter. Oligoribonucleotides were obtained that are at least 90% pure as assessed by CE for use in experiments described below. Compound identity was verified by matrix-assisted laser desorption ionization time-of-flight (MALDI-TOF) mass spectroscopy on a Voyager DE.TM. Biospectrometry Work Station (Applied Biosystems, Foster City, Calif.) following the manufacturer's recommended protocol. Relative molecular masses of all oligomers were obtained, often within 0.2% of expected molecular mass.

Preparation of Duplexes

Single-stranded RNA (ssRNA) oligomers were resuspended, e.g., at 100 μ M concentration in duplex buffer consisting of 100 mM potassium acetate, 30 mM HEPES, pH 7.5. Complementary sense and antisense strands were mixed in equal molar amounts to yield a final solution of, e.g., 50 μ M duplex. Samples were heated to 100°C for 5' in RNA buffer (IDT) and allowed to cool to room temperature before use. Double-stranded RNA (dsRNA)

oligomers were stored at -20°C. Single-stranded RNA oligomers were stored lyophilized or in nuclease-free water at -80°C.

Nomenclature

For consistency, the following nomenclature has been employed in the instant specification. Names given to duplexes indicate the length of the oligomers and the presence or absence of overhangs. A "25/27" is an asymmetric duplex having a 25 base sense strand and a 27 base antisense strand with a 2-base 3'-overhang. A "27/25" is an asymmetric duplex having a 27 base sense strand and a 25 base antisense strand.

Cell culture and RNA Transfection

HeLa cells were obtained from ATCC and maintained in DMEM (HyClone) supplemented with 10% fetal bovine serum (HyClone) at 37°C under 5% CO₂. HEPA1-6 cells were obtained from ATCC and maintained in DMEM (HyClone) supplemented with 10% fetal bovine serum (HyClone) at 37°C under 5% CO₂. For RNA transfections, cells were transfected with DsiRNAs as indicated at a final concentration of 1 nM, 0.3 nM or 0.1 nM using Lipofectamine™ RNAiMAX (Invitrogen) and following manufacturer's instructions. Briefly, for 0.1 nM transfections, e.g., of Example 3 below, an aliquot of stock solution of each DsiRNA was mixed with Opti-MEM I (Invitrogen) and Lipofectamine™ RNAiMAX to reach a volume of 200 µL. The resulting 200 µL mix was added per well into duplicate individual wells of 24 well plates and incubated for 20 min at RT to allow DsiRNA:Lipofectamine™ RNAiMAX complexes to form. Meanwhile, target cells were trypsinized and resuspended in medium. Finally, 300 µL of the cell suspension were added to each well (final volume 500 µL) and plates were placed into the incubator for 24 hours.

Assessment of EGFR Inhibition

EGFR target gene knockdown was determined by qRT-PCR, with values normalized to HPRT and SFRS9 housekeeping genes, and to transfections with control DsiRNAs and/or mock transfection controls.

RNA isolation and analysis

Media was aspirated, and total RNA was extracted using the SV96 kit (Promega). Approximately 100 ng of total RNA was reverse-transcribed using SuperscriptII, Oligo dT,

and random hexamers following manufacturer's instructions. Typically, one-sixth of the resulting cDNA was analyzed by qPCR using primers and probes specific for both the EGFR gene and for the human genes HPRT-1 and SFRS9. An ABI 7700 was used for the amplification reactions. Each sample was tested in triplicate. Relative EGFR RNA levels were normalized to HPRT1 and SFRS9 RNA levels and compared with RNA levels obtained in mock transfection control samples. Typically, one-fifteenth of the resulting cDNA was analyzed by qPCR using primers and probes specific for both the EGFR gene and for the human gene HPRT-1 or SFRS9. A Bio-Rad CFX96 was used for the amplification reactions. Each sample was tested in duplicate. Relative EGFR RNA levels were normalized to HPRT1 or SFRS9 RNA levels and compared with RNA levels obtained in mock transfection control samples.

Dose-Response Curves

NCI-H1975 cells were transfected *in vitro*, using lipid transfection reagent RNAiMAX, with a dose curve of the EGFR DsiRNAs derived *via* screening (or mock treated, without DsiRNA). One day post-transfection, lysates were made from the cells and total RNA was extracted using an SV 96 Total RNA Isolation System obtained from Promega. cDNA was made using a Roche Transcriptor First Strand cDNA Synthesis Kit (using Random Primers). qPCR was performed using BIO-RAD iQ Multiplex Powermix and primer probe sets for the EGFR gene and for the normalization gene SFRS9. Knockdown was determined relative to mock treatments, and data were analyzed using Prism software to determine IC50 values for each DsiRNA.

Assessment of Cell Growth Inhibition

NCI-H1975 cells were transfected *in vitro*, lipid transfection reagent RNAiMAX, with EGFR DsiRNAs derived from screening (or transfected with a control nonspecific DsiRNA, or mock treated, without DsiRNA). From one set of transfected cells, two days post-transfection, lysates were made from the cells and total RNA was extracted using a Promega SV 96 Total RNA Isolation System. cDNA was made using a Roche Transcriptor First Strand cDNA Synthesis Kit (using Random Primer). qPCR was performed with BIO-RAD iQ Multiplex Powermix and primer probe sets for the EGFR gene and for the normalization gene SFRS9. Knockdown was determined relative to mock treatments. A second identical set of

transfected cells were analyzed for cumulative cell growth five days after transfection, using a Promega Cell Titer Blue assay.

Example 2: DsiRNA Inhibition of EGFR – Primary Screen

DsiRNA molecules targeting EGFR were designed and synthesized as described above and tested in HeLa cells for inhibitory efficacy. For transfection, annealed DsiRNAs were mixed with the transfection reagent (Lipofectamine™ RNAiMAX, Invitrogen) in a volume of 50 µl/well and incubated for 20 minutes at room temperature. The HeLa (human) or HEPA1-6 (mouse) cells were trypsinized, resuspended in media, and added to wells (100uL per well) to give a final DsiRNA concentration of 1 nM in a volume of 150 µl. Each DsiRNA transfection mixture was added to 3 wells for triplicate DsiRNA treatments. Cells were incubated at 37°C for 24 hours in the continued presence of the DsiRNA transfection mixture. At 24 hours, RNA was prepared from each well of treated cells. The supernatants with the transfection mixtures were first removed and discarded, then the cells were lysed and RNA prepared from each well. Target EGFR RNA levels following treatment were evaluated by qRT-PCR for the EGFR target gene, with values normalized to those obtained for controls. Triplicate data was averaged and the % error determined for each treatment. Normalized data were graphed and the reduction of target mRNA by active DsiRNAs in comparison to controls was determined.

EGFR targeting DsiRNAs examined for EGFR inhibitory efficacy in a primary phase of testing are indicated in Tables 2 and 4 above, with results of such assays shown in Figures 2A-2D and in Tables 11 and 12 below. In this example, 356 asymmetric DsiRNAs (tested DsiRNAs possessed a 25/27mer structure) were constructed and tested for EGFR inhibitory efficacy in human HeLa and mouse HEPA1-6 cells incubated in the presence of such DsiRNAs at a concentration of 1 nM. The 356 asymmetric DsiRNAs tested included DsiRNAs selected from Tables 2 and 4 above, where sequences and structures of these tested asymmetric DsiRNAs are shown (in above Tables 2 and 4, underlined nucleotide residues indicate 2'-O-methyl modified residues, ribonucleotide residues are shown as UPPER CASE, and deoxyribonucleotide residues are shown as lower case).

Assay of the 356 EGFR targeting DsiRNAs in human HeLa and mouse HEPA1-6 cells at 1 nM revealed the following EGFR inhibitory efficacies, presented in Tables 11 and 12. EGFR levels were determined using qPCR assays positioned at indicated locations

within the EGFR transcript (for human HeLa cell experiments, paired qPCR assays were performed and are indicated as “Hs EGFR 1068-1232” (FAM) and “Hs EGFR 4704-4789” (Yakima Yellow); for mouse HEPA1-6 cell experiments, paired qPCR assays were performed and are indicated as “Mm EGFR 1955-2098” (Yakima Yellow) and “Mm EGFR 3602-3699” (FAM)).

Table 11: EGFR Inhibitory Efficacy of DsiRNAs Assayed at 1 nM in Human HeLa Cells

DsiRNA Name (Human EGFR Target Location)	Mouse EGFR Target Location	% Remaining EGFR mRNA $\pm$ % Error (Assay: Hs EGFR 1068-1232)	% Remaining EGFR mRNA $\pm$ % Error (Assay: Hs EGFR 4704-4789)
EGFR-31	N/A	170.2 $\pm$ 15.6	151.5 $\pm$ 12.6
EGFR-32	N/A	116.6 $\pm$ 3.8	97.6 $\pm$ 3.3
EGFR-34	N/A	111.8 $\pm$ 3.8	97.5 $\pm$ 5.9
EGFR-298	N/A	136.4 $\pm$ 3.9	133.6 $\pm$ 3.1
EGFR-300	N/A	77.8 $\pm$ 17.6	77.4 $\pm$ 8.5
EGFR-302	N/A	117.8 $\pm$ 8.8	106.4 $\pm$ 7.3
EGFR-390	N/A	19.8 $\pm$ 14	18 $\pm$ 9.2
EGFR-458	N/A	15.8 $\pm$ 16	14.6 $\pm$ 5.2
EGFR-463	497	67.6 $\pm$ 20.3	65.5 $\pm$ 3.7
EGFR-464	498	23.1 $\pm$ 12.3	21.4 $\pm$ 4.2
EGFR-489	N/A	32.5 $\pm$ 10.6	27.4 $\pm$ 9.8
EGFR-496	530	51 $\pm$ 8.7	46.7 $\pm$ 4.7
EGFR-497	531	49 $\pm$ 7.2	58.7 $\pm$ 5.3
EGFR-498	532	147.5 $\pm$ 15.8	128.7 $\pm$ 16.9
EGFR-499	533	48.6 $\pm$ 13.4	59.2 $\pm$ 16.3
EGFR-500	534	72.6 $\pm$ 17.1	77.7 $\pm$ 10.2
EGFR-501	535	122 $\pm$ 2.5	92.3 $\pm$ 5.9
EGFR-502	536	142.8 $\pm$ 3.6	114.8 $\pm$ 3.5
EGFR-503	537	82.4 $\pm$ 11.6	79.4 $\pm$ 5.7
EGFR-504	538	70.3 $\pm$ 6.2	75.9 $\pm$ 5
EGFR-505	539	71.5 $\pm$ 5.7	73.7 $\pm$ 7.7
EGFR-506	540	96.7 $\pm$ 13.1	95.2 $\pm$ 10.4
EGFR-507	541	45.3 $\pm$ 2.1	52.1 $\pm$ 2.2
EGFR-508	542	71.5 $\pm$ 18.3	71.5 $\pm$ 12.9
EGFR-509	543	32.7 $\pm$ 6.9	25.3 $\pm$ 6.1
EGFR-525	N/A	21.6 $\pm$ 19.6	19.5 $\pm$ 3.2
EGFR-676	N/A	27.9 $\pm$ 13.3	23.8 $\pm$ 12.4
EGFR-701	N/A	47.4 $\pm$ 6.8	34.3 $\pm$ 6.3
EGFR-707	N/A	26 $\pm$ 5.7	29.5 $\pm$ 1.6
EGFR-707	N/A	30.8 $\pm$ 4.9	22.6 $\pm$ 7.8
EGFR-709	N/A	39.7 $\pm$ 6.6	35.5 $\pm$ 8.5
EGFR-710	N/A	47.4 $\pm$ 14.6	39.8 $\pm$ 9.5
EGFR-827	N/A	22.4 $\pm$ 6	26.6 $\pm$ 4.9
EGFR-838	872	86.3 $\pm$ 14	85.9 $\pm$ 10.1
EGFR-839	873	58.2 $\pm$ 8.2	58.1 $\pm$ 8.4
EGFR-840	874	56.7 $\pm$ 9.6	62.2 $\pm$ 6

EGFR-841	875	57.4 ± 11	63.4 ± 8.9
EGFR-842	876	59.6 ± 20.1	60.5 ± 11
EGFR-876	910	19.5 ± 15.7	20.5 ± 11.2
EGFR-877	911	15.7 ± 35.7	18.3 ± 13.9
EGFR-878	912	20.8 ± 8.5	18.3 ± 3.8
EGFR-879	913	58.2 ± 9.7	42.7 ± 8.1
EGFR-899	933	121.8 ± 14.2	103.9 ± 13.4
EGFR-900	934	81.4 ± 7.7	70.4 ± 7.5
EGFR-901	935	89.5 ± 5.1	70.4 ± 4.4
EGFR-902	936	88.9 ± 15.1	61.9 ± 12.4
EGFR-903	937	71.6 ± 18.3	69 ± 9.5
EGFR-904	938	92.6 ± 17.1	77.5 ± 20.3
EGFR-905	939	132.4 ± 9.6	97.5 ± 4.4
EGFR-912	N/A	63.7 ± 25.8	69.5 ± 22.2
EGFR-914	N/A	159.5 ± 19.7	120.9 ± 16.3
EGFR-926	N/A	95.8 ± 8.7	100.3 ± 10.1
EGFR-954	988	122 ± 14.2	93.6 ± 4.7
EGFR-955	989	61.8 ± 4.9	48.1 ± 9.4
EGFR-956	990	90.2 ± 15	67.6 ± 11.6
EGFR-1005	N/A	130.7 ± 6.3	56.3 ± 5.2
EGFR-1013	N/A	21.5 ± 7.3	32.2 ± 14.8
EGFR-1175	N/A	136.5 ± 6.1	130.4 ± 7.7
EGFR-1271	N/A	11.4 ± 16.8	12.6 ± 6.4
EGFR-1286	N/A	19.4 ± 3.4	21.9 ± 5
EGFR-1313	1347	11.5 ± 9.3	11.5 ± 10
EGFR-1330	N/A	9.2 ± 5.6	12.6 ± 3.7
EGFR-1437	N/A	32.2 ± 22.6	32 ± 15.7
EGFR-1475	N/A	59.1 ± 8	57.5 ± 8
EGFR-1480	1514	105.7 ± 22.3	82.5 ± 21
EGFR-1481	1515	98.2 ± 14.8	84.9 ± 13.8
EGFR-1482	1516	97.7 ± 9.7	81.7 ± 5.6
EGFR-1483	1517	152.6 ± 8.8	100.6 ± 4.5
EGFR-1484	1518	151.4 ± 18.4	125.7 ± 19.7
EGFR-1485	1519	103 ± 7	91.2 ± 6.7
EGFR-1486	1520	97.2 ± 6.7	76.2 ± 3.7
EGFR-1487	1521	81.4 ± 19.9	60.4 ± 13.2
EGFR-1561	1595	36.9 ± 11.2	25.2 ± 11.1
EGFR-1562	1596	25.9 ± 4.5	16.2 ± 4.7
EGFR-1563	1597	15.9 ± 8.3	11.1 ± 8.3
EGFR-1661	N/A	54.4 ± 4.4	43.9 ± 8.8
EGFR-1679	N/A	15.8 ± 15.3*	15.9 ± 8.5*

EGFR-1691	1725	39.1 ± 6.4	21.3 ± 4.8
EGFR-1723	N/A	20.4 ± 10.4	14 ± 7.9
EGFR-1838	N/A	36.3 ± 10.5	29.4 ± 6.2
EGFR-1963	1997	45.1 ± 55.6	62.1 ± 20.9
EGFR-1964	1998	81.8 ± 6.2	77 ± 2.3
EGFR-2008	2042	63.5 ± 5.5	63.4 ± 7.4
EGFR-2009	2043	$32.1 \pm 7.4^*$	$34.6 \pm 6^*$
EGFR-2010	2044	52.8 ± 4.3	46.5 ± 6.6
EGFR-2011	2045	25.3 ± 3.7	27.9 ± 5.4
EGFR-2012	2046	47.1 ± 15.3	51.8 ± 14.6
EGFR-2227	N/A	76.7 ± 11.1	85 ± 8.2
EGFR-2228	N/A	86 ± 3.9	86.5 ± 2.9
EGFR-2232	N/A	141.2 ± 5.6	127.4 ± 7.4
EGFR-2233	N/A	80 ± 11	71.3 ± 11.3
EGFR-2295	N/A	103.7 ± 4.6	89.4 ± 4.3
EGFR-2298	N/A	145 ± 17.4	131.4 ± 12
EGFR-2399	N/A	36.7 ± 5.3	30.9 ± 2.5
EGFR-2401	2441	62.7 ± 4.1	45.6 ± 8.3
EGFR-2402	2442	85.2 ± 6	87.4 ± 6.6
EGFR-2417	N/A	$70 \pm 7.8^*$	$78.3 \pm 11.4^*$
EGFR-2419	N/A	57.5 ± 6.6	61.4 ± 8.1
EGFR-2420	N/A	69.6 ± 6.7	68.9 ± 6.1
EGFR-2421	N/A	160.1 ± 15.8	155.7 ± 5.6
EGFR-2422	N/A	112.5 ± 6.3	82.2 ± 3.8
EGFR-2458	2498	23.9 ± 16	18.6 ± 7
EGFR-2459	2499	39.6 ± 10.6	35.3 ± 6.7
EGFR-2460	2500	18.3 ± 5.6	16.7 ± 4.6
EGFR-2461	2501	22.4 ± 14.6	16.4 ± 11.2
EGFR-2462	2502	13.2 ± 6.7	10.5 ± 4.9
EGFR-2463	2503	14.6 ± 14	11.6 ± 8.1
EGFR-2464	2504	26.7 ± 3.7	12.9 ± 3.1
EGFR-2465	2505	16.6 ± 31.9	14.7 ± 7.3
EGFR-2591	N/A	77.9 ± 13.3	83.2 ± 10
EGFR-2592	N/A	118.6 ± 10.2	123.7 ± 10.6
EGFR-2594	N/A	102.8 ± 2.1	97.5 ± 2.6
EGFR-2624	N/A	28.5 ± 12.9	25.2 ± 11.1
EGFR-2627	N/A	135.2 ± 6.9	103.4 ± 10.2
EGFR-2631	N/A	73.7 ± 6.2	67 ± 2.7
EGFR-2632	N/A	123.1 ± 3.1	104.1 ± 5.5
EGFR-2643	N/A	68.1 ± 2.3	66.3 ± 2.7
EGFR-2644	N/A	85.2 ± 5.4	79.5 ± 4.3

EGFR-2754	N/A	68.5 ± 7.1	58.4 ± 6.8
EGFR-2756	N/A	75.8 ± 20.5	69.2 ± 12.4
EGFR-2757	N/A	104.3 ± 4.8	99.6 ± 3.9
EGFR-2758	N/A	116.8 ± 13	109.2 ± 1.5
EGFR-2760	N/A	61.1 ± 4.6	59 ± 5.2
EGFR-2762	N/A	59.4 ± 7.7	54.3 ± 8.8
EGFR-2764	N/A	68.6 ± 9.4	74.1 ± 4.6
EGFR-2765	N/A	133.7 ± 4.2	117.7 ± 3.8
EGFR-2767	N/A	70 ± 8.4	86.5 ± 5
EGFR-2815	2855	30.5 ± 13.7	19.7 ± 11.5
EGFR-2816	2856	20.4 ± 5.8	14.7 ± 5.8
EGFR-2817	2857	23.8 ± 9.6	18.9 ± 6.8
EGFR-2818	2858	22.8 ± 2.9	16.5 ± 3.8
EGFR-2819	2859	23.4 ± 13.5	19.5 ± 10.7
EGFR-2820	2860	54.4 ± 5.3	46.9 ± 8.2
EGFR-2821	2861	49.2 ± 5.6	35.4 ± 1.7
EGFR-2822	2862	182.2 ± 1.1	130.5 ± 1.7
EGFR-2823	2863	105 ± 16.3	80.5 ± 14.5
EGFR-2824	2864	67.7 ± 5.8	77.3 ± 6
EGFR-2825	2865	66.8 ± 8.7	63.3 ± 10
EGFR-2826	2866	106 ± 13.1	111.6 ± 13
EGFR-2827	2867	116 ± 7	96.8 ± 4.7
EGFR-2828	2868	100 ± 3.1	84.2 ± 6.9
EGFR-2829	2869	48.7 ± 8.3	45.4 ± 8
EGFR-2830	2870	57.4 ± 9.2	72.9 ± 7.8
EGFR-2831	2871	44.5 ± 13.2	51.7 ± 14.1
EGFR-2832	2872	74.7 ± 7.5	72.8 ± 6.7
EGFR-2833	2873	80 ± 3.5	66.3 ± 6.6
EGFR-2834	2874	109.6 ± 10	93.2 ± 8.7
EGFR-2835	2875	88.4 ± 5.7	79.1 ± 4.1
EGFR-2836	2876	85.9 ± 7.7	76.6 ± 2.8
EGFR-2837	2877	77.5 ± 7.5	59.9 ± 4.7
EGFR-2891	2931	62.7 ± 7.9	55.2 ± 7.3
EGFR-2892	2932	31.2 ± 3	25.1 ± 3
EGFR-2893	2933	33.3 ± 10.3	32.6 ± 4.2
EGFR-2894	2934	38.4 ± 10.2	29 ± 8.2
EGFR-2895	2935	43.6 ± 14.3	37.8 ± 5.8
EGFR-2896	2936	52.8 ± 9.5	45 ± 3.1
EGFR-2897	2937	20.9 ± 13.3	19.6 ± 10.2
EGFR-2915	N/A	14.7 ± 14.5	10 ± 9.5
EGFR-3088	3128	26.7 ± 4.8	18.5 ± 6.8

EGFR-3089	3129	33.6 ± 22.7	27.7 ± 4.3
EGFR-3090	3130	29.9 ± 18.2	19.8 ± 17.2
EGFR-3091	3131	34.8 ± 22.5	26.4 ± 22
EGFR-3092	3132	$18.4 \pm 26.6^*$	$12.2 \pm 15.8^*$
EGFR-3093	3133	73.5 ± 16	49.5 ± 17.1
EGFR-3094	3134	17.8 ± 21.1	14.3 ± 21.7
EGFR-3095	3135	25.4 ± 13.3	20.8 ± 16.9
EGFR-3096	3136	71.7 ± 15.6	45.9 ± 17.2
EGFR-3097	3137	38.1 ± 8.1	29.1 ± 8.8
EGFR-3098	3138	33.6 ± 13.2	30.3 ± 5.4
EGFR-3099	3139	76.8 ± 14.5	60 ± 10.5
EGFR-3100	3140	35 ± 6.5	30.9 ± 3.9
EGFR-3101	3141	44 ± 5.7	33 ± 4.4
EGFR-3102	3142	28.7 ± 11.3	24.6 ± 10.4
EGFR-3103	3143	22.6 ± 12.2	19.1 ± 9.8
EGFR-3104	3144	50.4 ± 7.2	36.9 ± 3.3
EGFR-3105	3145	19 ± 11.7	15.3 ± 5.5
EGFR-3106	3146	29.2 ± 10.1	22.6 ± 5
EGFR-3107	3147	22.9 ± 15.4	22 ± 9
EGFR-3108	3148	15 ± 6.4	10.1 ± 4.3
EGFR-3109	3149	21.7 ± 22.6	14.7 ± 12.4
EGFR-3110	3150	13.1 ± 11.7	10.3 ± 7.3
EGFR-3111	3151	11 ± 3.7	12.2 ± 4.3
EGFR-3112	3152	19.7 ± 3.1	11.1 ± 3.1
EGFR-3113	3153	35.2 ± 12.2	34.6 ± 13.4
EGFR-3115	N/A	$20.7 \pm 8.1^*$	$20.1 \pm 6.7^*$
EGFR-3117	N/A	21.3 ± 5.7	22 ± 6.6
EGFR-3118	N/A	18.4 ± 6.7	13.4 ± 6.7
EGFR-3120	N/A	26.3 ± 9.8	23.9 ± 8.9
EGFR-3169	3209	63 ± 21.1	67.2 ± 15.3
EGFR-3170	3210	92.8 ± 7.6	78.2 ± 10.3
EGFR-3220	3260	27.7 ± 6.9	31.9 ± 7.8
EGFR-3221	3261	30.2 ± 10.5	18.8 ± 7.4
EGFR-3222	3262	15.2 ± 11.2	14.2 ± 11.4
EGFR-3223	3263	17.6 ± 17.1	15.2 ± 11.5
EGFR-3224	3264	23.1 ± 18.4	24.2 ± 7.9
EGFR-3372	N/A	24.8 ± 18.7	20.5 ± 18.6
EGFR-3375	N/A	26.2 ± 24.5	27.6 ± 9.4
EGFR-3440	N/A	63 ± 5.9	56.9 ± 6.4
EGFR-3441	N/A	76.5 ± 7.7	70.1 ± 6.3
EGFR-3457	N/A	51.7 ± 15.6	36 ± 8.7

EGFR-3458	N/A	67.4 ± 6.2	52.4 ± 6
EGFR-3459	N/A	20.6 ± N/A	28.2 ± N/A
EGFR-3460	N/A	81.3 ± 1.7	70.6 ± 3.7
EGFR-3461	N/A	102 ± 7.1	79.9 ± 5.1
EGFR-3463	N/A	44.7 ± 11.6	34.3 ± 2.8
EGFR-3772	3806	29.3 ± 16.5	26.3 ± 12.8
EGFR-3773	3807	30.4 ± 18	34 ± 5.6
EGFR-3774	3808	30.9 ± 1.8	19.6 ± 2
EGFR-3775	3809	18.2 ± 11.6	19.1 ± 3.9
EGFR-3776	3810	23.8 ± 3.2	15.6 ± 4.9
EGFR-3777	3811	14.2 ± 5.9	13.3 ± 2.5
EGFR-3778	3812	20.3 ± 8	18.8 ± 2.8
EGFR-3779	3813	27.3 ± 3.5	25.8 ± 9.5
EGFR-3876	N/A	23.2 ± 10.3	22.5 ± 5
EGFR-4178	N/A	38.1 ± 6.8	22.6 ± 6.9
EGFR-4205	N/A	43.3 ± 12.6	34.3 ± 7.8
EGFR-4249	N/A	26.5 ± 2.9	10.4 ± 2.6
EGFR-4284	N/A	67.3 ± 5.2	53.2 ± 6.2
EGFR-4285	N/A	61.9 ± 8.4	42.1 ± 9.5
EGFR-4286	N/A	85.6 ± 8.8	71.8 ± 4.9
EGFR-4287	N/A	59.5 ± 1.8	41.8 ± 2.8
EGFR-4288	N/A	73.8 ± 15.4	60.6 ± 11.2
EGFR-4290	N/A	79.7 ± 13.4	73.9 ± 9.9
EGFR-4291	N/A	59.9 ± 9	42.6 ± 11.4
EGFR-4292	N/A	56.4 ± 5.7	30.6 ± 4.3
EGFR-4293	N/A	60.1 ± 7.2	40.5 ± 7.5
EGFR-4294	N/A	58.3 ± 5.4	52 ± 4.7
EGFR-4295	N/A	46 ± 8.1	29.2 ± 3.7
EGFR-4372	N/A	44.8 ± 9.6	27.1 ± 3.6
EGFR-4373	N/A	33.2 ± 11.9	33.7 ± 7.3
EGFR-4450	N/A	35 ± 7.5	14.9 ± 8.9
EGFR-4455	N/A	27.3 ± 6.9	12.7 ± 4.6
EGFR-4550	N/A	18.2 ± 5	12 ± 4
EGFR-4684	N/A	65.9 ± 7.9	36.8 ± 6.3
EGFR-4804	N/A	34.8 ± 5.7	15.1 ± 2.6
EGFR-4806	N/A	24.7 ± 10.4	7.8 ± 4.6
EGFR-4807	N/A	43.3 ± N/A	12.4 ± N/A
EGFR-4808	N/A	63 ± 4.6	15.2 ± 6.5
EGFR-4809	N/A	40.6 ± 11.5	15 ± 11.9
EGFR-4810	N/A	38.9 ± 9.2	14.6 ± 10.1
EGFR-4811	N/A	26.8 ± 7.8	10.4 ± 9.9

EGFR-4812	N/A	34.7 ± 10.2	10.5 ± 10.6
EGFR-4813	N/A	38.7 ± 7.1	11.3 ± 4.3
EGFR-4816	N/A	28.1 ± 7.7	11 ± 7.3
EGFR-4817	N/A	24.4 ± 10.9	11.1 ± 4.8
EGFR-4818	N/A	41.6 ± 11.2	18 ± 8.2
EGFR-4819	N/A	24.3 ± 15.9	14.5 ± 14.3
EGFR-4824	N/A	39.7 ± 3.1	15.9 ± 3.2
EGFR-4953	N/A	26.6 ± 7.2	14.1 ± 5.7
EGFR-4970	N/A	38.8 ± 9.4	18.7 ± 8.2
EGFR-5003	N/A	30.7 ± 12	16.8 ± 7.6
EGFR-5206	N/A	24.6 ± 17.9	13.6 ± 18.1
EGFR-5275	N/A	50.5 ± 2.8	40.5 ± 4.3
EGFR-5374	N/A	45.3 ± 12.1	34.2 ± 5.7
EGFR-5429	N/A	54.2 ± 12.5	49.8 ± 6.7
EGFR-5497	N/A	36.1 ± 2.3	25.9 ± 1.4
EGFR-5505	N/A	36.1 ± 20.7	25.8 ± 19.1
EGFR-5506	N/A	29.2 ± 5.4	19.4 ± 2.5
EGFR-5512	N/A	68.9 ± 9.8	52.3 ± 7.3
EGFR-5565	N/A	42.6 ± 10.2	34 ± 5.9

* Only normalized to SFRS9

The following DsiRNAs were observed to reduce EGFR levels by 70% or more when administered to mammalian cells (here, human HeLa cells) at 1nM: EGFR-390, EGFR-458, EGFR-464, EGFR-525, EGFR-676, EGFR-707, EGFR-827, EGFR-876, EGFR-877, EGFR-878, EGFR-1271, EGFR-1286, EGFR-1313, EGFR-1330, EGFR-1562, EGFR-1563, EGFR-1679, EGFR-1723, EGFR-2011, EGFR-2458, EGFR-2460, EGFR-2461, EGFR-2462, EGFR-2463, EGFR-2464, EGFR-2465, EGFR-2624, EGFR-2816, EGFR-2817, EGFR-2818, EGFR-2819, EGFR-2897, EGFR-2915, EGFR-3088, EGFR-3090, EGFR-3092, EGFR-3094, EGFR-3095, EGFR-3102, EGFR-3103, EGFR-3105, EGFR-3106, EGFR-3107, EGFR-3108, EGFR-3109, EGFR-3110, EGFR-3111, EGFR-3112, EGFR-3115, EGFR-3117, EGFR-3118, EGFR-3120, EGFR-3222, EGFR-3223, EGFR-3224, EGFR-3372, EGFR-3375, EGFR-3459, EGFR-3772, EGFR-3775, EGFR-3776, EGFR-3777, EGFR-3778, EGFR-3779, EGFR-3876, EGFR-4249, EGFR-4455, EGFR-4550, EGFR-4806, EGFR-4811, EGFR-4816, EGFR-4817, EGFR-4819, EGFR-4953, EGFR-5206 and EGFR-5506.

Among these DsiRNAs, the following DsiRNAs were observed to reduce EGFR levels by 80% or more when administered at 1nM: EGFR-390, EGFR-458, EGFR-877, EGFR-1271, EGFR-1313, EGFR-1330, EGFR-1563, EGFR-1679, EGFR-2460, EGFR-2462, EGFR-2463, EGFR-2465, EGFR-2915, EGFR-3092, EGFR-3094, EGFR-3105, EGFR-3108, EGFR-3110, EGFR-3111, EGFR-3112, EGFR-3118, EGFR-3222, EGFR-3223, EGFR-3775, EGFR-3777 and EGFR-4550.

Table 12: EGFR Inhibitory Efficacy of DsiRNAs Assayed at 1 nM in Mouse HEPA1-6 Cells

DsiRNA Name (Human EGFR Target Location)	Mouse EGFR Target Location/DsiRNA Name	% Remaining EGFR mRNA $\pm$ % Error (Assay: Mm EGFR 1955-2098)	% Remaining EGFR mRNA $\pm$ % Error (Assay: Mm EGFR 3602-3699)
EGFR-463	497	95.8 $\pm$ 20	103.7 $\pm$ 11
EGFR-464	498	42.6 $\pm$ 8.5	48.5 $\pm$ 5.8
EGFR-496	530	82.3 $\pm$ 2.3	82.2 $\pm$ 1.9
EGFR-497	531	97.7 $\pm$ 1.6	107.9 $\pm$ 2.7
EGFR-498	532	114.7 $\pm$ 8.1	119.8 $\pm$ 6.6
EGFR-499	533	101.5 $\pm$ 3.7	113.3 $\pm$ 1.9
EGFR-500	534	127 $\pm$ 11.9	126.1 $\pm$ 6.6
EGFR-501	535	105.3 $\pm$ 4.8	135.7 $\pm$ 3.4
EGFR-502	536	108.6 $\pm$ 2.7	96.1 $\pm$ 2.3
EGFR-503	537	99.5 $\pm$ 7.3	95.7 $\pm$ 4.1
EGFR-504	538	100.9 $\pm$ 2.3	104 $\pm$ 5.3
EGFR-505	539	72.6 $\pm$ 5.5	100.2 $\pm$ 8.3
EGFR-506	540	94.4 $\pm$ 17.8	116.9 $\pm$ 2.2
EGFR-507	541	100.7 $\pm$ 6	109.6 $\pm$ 3.3
EGFR-508	542	123.7 $\pm$ 4	120.4 $\pm$ 3.2
EGFR-509	543	118.1 $\pm$ 3.5	114.5 $\pm$ 1.9
EGFR-838	872	109.7 $\pm$ 11.7	97.3 $\pm$ 5.4
EGFR-839	873	79.2 $\pm$ 2.3	78.7 $\pm$ 3.7
EGFR-840	874	73 $\pm$ 9.5	73.9 $\pm$ 5.4
EGFR-841	875	80.7 $\pm$ 9.3	99.5 $\pm$ 2.9
EGFR-842	876	84.6 $\pm$ 14.3	95.9 $\pm$ 4.3
EGFR-876	910	69.2 $\pm$ 10.4	79.9 $\pm$ 4.7
EGFR-877	911	84.7 $\pm$ 5.8	91.3 $\pm$ 5.1
EGFR-878	912	78.2 $\pm$ 10.1	83.8 $\pm$ 5.7
EGFR-879	913	114.8 $\pm$ 2.6	111.4 $\pm$ 2.4
EGFR-899	933	137.2 $\pm$ 11.5	145.3 $\pm$ 7.4
EGFR-900	934	89.9 $\pm$ 5.4	118.7 $\pm$ 2.6

EGFR-901	935	108.4 ± 8.3	105.3 ± 9.1
EGFR-902	936	95.4 ± 4.5	91.8 ± 3.4
EGFR-903	937	101.2 ± 3.2	121 ± 9
EGFR-904	938	142.2 ± 10.4	157.1 ± 9.3
EGFR-905	939	134.5 ± 9.7	135.9 ± 3.9
EGFR-954	988	131.1 ± 13	119 ± 2
EGFR-955	989	103.4 ± 6.8	119.7 ± 11.2
EGFR-956	990	86.7 ± 6.1	106.3 ± 2.7
EGFR-1313	1347	75.4 ± 24.1	83.8 ± 13.8
EGFR-1480	1514	120.1 ± 5.7	102.5 ± 5.2
EGFR-1481	1515	147.3 ± 6.7	148.6 ± 4.4
EGFR-1482	1516	110 ± 22.1	139.3 ± 18.1
EGFR-1483	1517	142.9 ± 2.3	128.2 ± 1.2
EGFR-1484	1518	136.9 ± 0.8	118.2 ± 1.1
EGFR-1485	1519	121.1 ± 3.2	116.2 ± 4.4
EGFR-1486	1520	97.3 ± 6.5	108.2 ± 6.5
EGFR-1487	1521	116.6 ± 1.5	100.2 ± 3.7
EGFR-1561	1595	95.4 ± 1.2	82.9 ± 4.5
EGFR-1562	1596	43.2 ± 7.8	49 ± 6.4
EGFR-1563	1597	78.7 ± 7.8	79.6 ± 4.4
EGFR-1691	1725	87.2 ± 4.9	87.2 ± 3.2
EGFR-1963	1997	57.1 ± N/A	74.9 ± N/A
EGFR-1964	1998	104.8 ± 9.6	109.1 ± 9.2
EGFR-2008	2042	101.2 ± 4.8	122.7 ± 2.8
EGFR-2009	2043	77.2 ± 9.4	98.5 ± 3.5
EGFR-2010	2044	103.4 ± 10.7	131.8 ± 6.9
EGFR-2011	2045	93.6 ± 5	113.6 ± 7.3
EGFR-2012	2046	87.5 ± 6	127.3 ± 9.2
EGFR-2401	2441	104.9 ± 5.4	121.9 ± 2.9
EGFR-2402	2442	66.8 ± 23.1	79.5 ± 8.8
EGFR-2458	2498	60.5 ± 2.1	53.7 ± 2.5
EGFR-2459	2499	82.9 ± 5.2	89.9 ± 7.5
EGFR-2460	2500	48.9 ± 6.4	44 ± 2.4
EGFR-2461	2501	70.8 ± 5.4	67.7 ± 4.3
EGFR-2462	2502	32.9 ± 20.3	29.2 ± 15.5
EGFR-2463	2503	34.3 ± 23.2	45.8 ± 7.3
EGFR-2464	2504	68.9 ± 3.3	67.3 ± 2.4
EGFR-2465	2505	66.3 ± 9.5	55.3 ± 6.5
EGFR-2815	2855	83.1 ± 6.5	70.4 ± 6.8
EGFR-2816	2856	68.7 ± 2	60.2 ± 3.8
EGFR-2817	2857	67.3 ± 5.3	58.6 ± 1
EGFR-2818	2858	62.2 ± 3.8	56.2 ± 7.8
EGFR-2819	2859	54.9 ± 14.2	55.6 ± 3.3

EGFR-2820	2860	94.8 ± 7.6	98.2 ± 6.7
EGFR-2821	2861	89.9 ± 2.2	94.7 ± 2.3
EGFR-2822	2862	134 ± 17.5	110.6 ± 16.7
EGFR-2823	2863	127.6 ± 6.7	113 ± 6.2
EGFR-2824	2864	112.7 ± 3.4	108.4 ± 4
EGFR-2825	2865	90.1 ± 7.7	103.9 ± 7.6
EGFR-2826	2866	130.8 ± 1.6	121.6 ± 1.9
EGFR-2827	2867	108.2 ± 8.3	107.4 ± 7.3
EGFR-2828	2868	122.4 ± 9	118 ± 3.3
EGFR-2829	2869	112.1 ± 2.3	125.1 ± 3.8
EGFR-2830	2870	101.4 ± 6.3	102.8 ± 5
EGFR-2831	2871	103.5 ± 4.6	105.4 ± 1.6
EGFR-2832	2872	94.4 ± 17.6	101.1 ± 11.2
EGFR-2833	2873	73.9 ± 22.1	100.2 ± 11.3
EGFR-2834	2874	119.5 ± 15	108.3 ± 9.1
EGFR-2835	2875	114.9 ± 7.2	118.7 ± 6.3
EGFR-2836	2876	142.4 ± 6.1	137.8 ± 1.6
EGFR-2837	2877	146.1 ± 4.4	140.5 ± 3
EGFR-2891	2931	72.1 ± 6	57.1 ± 4
EGFR-2892	2932	73.9 ± 3	55.1 ± 7.5
EGFR-2893	2933	64.1 ± 12.1	56.5 ± 5.7
EGFR-2894	2934	65.4 ± 1	75.2 ± 3.5
EGFR-2895	2935	88.4 ± 13.9	81 ± 4.1
EGFR-2896	2936	74.7 ± 14.7	86.9 ± 4.6
EGFR-2897	2937	82.3 ± 7.6	69.3 ± 1.6
EGFR-3088	3128	74.2 ± 2.3	55.1 ± 3.3
EGFR-3089	3129	29.1 ± 31	31.9 ± 12.8
EGFR-3090	3130	64.4 ± 12.5	48.6 ± 8.8
EGFR-3091	3131	77.5 ± 1	67.7 ± 1.7
EGFR-3092	3132	86.7 ± 4.5	76.8 ± 7.6
EGFR-3093	3133	91 ± N/A	100.8 ± N/A
EGFR-3094	3134	57.2 ± 4.6	47.1 ± 5.6
EGFR-3095	3135	85.4 ± 7.9	76.9 ± 8.8
EGFR-3096	3136	87.3 ± 2.3	73.5 ± 2.5
EGFR-3097	3137	51.5 ± 10.9	41.8 ± 1.4
EGFR-3098	3138	67.1 ± 7.9	63.6 ± 2.3
EGFR-3099	3139	101.2 ± 9.9	94.9 ± 6.8
EGFR-3100	3140	68 ± 13.3	64.6 ± 5.3
EGFR-3101	3141	92.2 ± 5	96.9 ± 8.2
EGFR-3102	3142	77.3 ± 12.1	74.1 ± 9.1
EGFR-3103	3143	69.7 ± 8	60.7 ± 9.7
EGFR-3104	3144	84.8 ± 2.1	78.9 ± 3
EGFR-3105	3145	42.8 ± 5.5	26.1 ± 3.1

EGFR-3106	3146	63 ± 6.9	51.5 ± 6.1
EGFR-3107	3147	60.2 ± 11.1	49.4 ± 5.7
EGFR-3108	3148	48.6 ± 1.8	33.9 ± 2.4
EGFR-3109	3149	46.6 ± 3	37.1 ± 7.6
EGFR-3110	3150	38 ± 9.7	26.3 ± 3.4
EGFR-3111	3151	46.5 ± 4	30.9 ± 11.5
EGFR-3112	3152	45.3 ± 7	28.8 ± 5.4
EGFR-3113	3153	100.5 ± 16.4	80.1 ± 5.4
EGFR-3169	3209	122.6 ± 3.5	104.1 ± 2.7
EGFR-3170	3210	116.6 ± 11.4	119.3 ± 10.3
EGFR-3220	3260	86.2 ± 13.1	81.4 ± 8
EGFR-3221	3261	69.6 ± 1.5	53.5 ± 4.5
EGFR-3222	3262	54.9 ± 3.6	40.3 ± 6.2
EGFR-3223	3263	75.5 ± 4.6	56.2 ± 7.4
EGFR-3224	3264	81.6 ± 3.8	68.9 ± 3.7
EGFR-3772	3806	87.1 ± 6.8	53.9 ± 9.7
EGFR-3773	3807	93.9 ± 3.9	67.1 ± 2.9
EGFR-3774	3808	72.3 ± 8.7	49.7 ± 9.6
EGFR-3775	3809	75.6 ± 21.4	48.8 ± 29.3
EGFR-3776	3810	70.8 ± 4	48.5 ± 1.7
EGFR-3777	3811	66 ± 9.5	43 ± 9.2
EGFR-3778	3812	71 ± 3.6	52.6 ± 5.2
EGFR-3779	3813	99.7 ± 2.4	72.4 ± 3.2
	EGFR-m71	89.7 ± 9.9	74.8 ± 6.9
	EGFR-m78	42.5 ± 13.8	55.3 ± 5.8
	EGFR-m87	84.5 ± 2.9	114 ± 2.8
	EGFR-m90	81.3 ± 6.3	72.1 ± 5
	EGFR-m92	81.7 ± 3.6	85.4 ± 4.3
	EGFR-m94	74.8 ± 3.4	79.3 ± 2.9
	EGFR-m97	96 ± 7.7	131.7 ± 6.2
	EGFR-m99	98.6 ± 6	120.5 ± 1.9
	EGFR-m100	85.4 ± 3.5	71.9 ± 3.6
	EGFR-m101	97.5 ± 3.3	115.2 ± 3.1
	EGFR-m111	100.3 ± 4	116.2 ± 4.4
	EGFR-m114	99 ± 10.5	105 ± 4.3
	EGFR-m333	85 ± 5.9	132.4 ± 2
	EGFR-m334	86.6 ± 5.9	109.1 ± 3.9
	EGFR-m335	74.6 ± 3.7	82.8 ± 3.7
	EGFR-m336	78.1 ± 3.3	91.4 ± 3.4
	EGFR-m337	61.1 ± 4.7	87.9 ± 5.1
	EGFR-m338	35.8 ± N/A	37.7 ± N/A
	EGFR-m339	74 ± 4.9	78 ± 5.8
	EGFR-m341	69.5 ± 3.4	90.8 ± 2.6

EGFR-m342	104.2 ± 10.1	135 ± 4.6
EGFR-m343	112.7 ± 11.1	105.6 ± 2.2
EGFR-m344	107.5 ± 1.8	89.9 ± 2.6
EGFR-m347	107.9 ± 6.8	127.7 ± 7.2
EGFR-m348	98.5 ± 8.3	86.1 ± 3.9
EGFR-m734	51.9 ± 7.9	38.3 ± 5.6
EGFR-m735	52.5 ± 2.4	57.7 ± 3.8
EGFR-m736	40.8 ± 4.8	39.6 ± 2.3
EGFR-m738	81 ± 2.9	90.3 ± 5.3
EGFR-m740	86.7 ± 6.2	99.4 ± 4.7
EGFR-m741	91.3 ± 2.4	78 ± 3
EGFR-m879	48.1 ± 16.2	52.2 ± 8
EGFR-m948	76.3 ± N/A	81 ± N/A
EGFR-m1154	71.7 ± 4.3	98 ± 8.7
EGFR-m1302	24.4 ± 10.6	51.9 ± 13.7
EGFR-m1439	79.9 ± 6.5	89.4 ± 2.7
EGFR-m1509	70.7 ± 1.5	83.9 ± 4.8
EGFR-m1526	72.5 ± 2.3	79 ± 5
EGFR-m1528	43 ± 2.6	43.8 ± 5.4
EGFR-m1531	77 ± 2.2	66.9 ± 1.4
EGFR-m2168	76.9 ± 23.1	80.1 ± 7.9
EGFR-m2253	102.1 ± 3.1	83.9 ± 0.9
EGFR-m2286	99.8 ± 9.9	107.5 ± 7.3
EGFR-m2301	66.5 ± 8.3	88.7 ± 21.3
EGFR-m2350	52.4 ± 3.1	48.6 ± 5
EGFR-m2351	86.6 ± 8.3	61.2 ± 15.3
EGFR-m2352	83.5 ± 1.5	75.1 ± 2.2
EGFR-m2617	115 ± 9.5	99.9 ± 9.2
EGFR-m2631	115.6 ± 8.6	129.2 ± 10.9
EGFR-m2683	64.9 ± 13.8	66.3 ± 8.2
EGFR-m2684	107.1 ± 7.9	135.8 ± 16.3
EGFR-m2800	81.6 ± 19.2	76.7 ± 12.1
EGFR-m2805	89.3 ± 6.3	91.3 ± 1.4
EGFR-m2879	83.1 ± 3.1	81.7 ± 3
EGFR-m2880	100.8 ± 1.3	80.7 ± 2.3
EGFR-m2882	105.3 ± 6.2	125.6 ± 6.6
EGFR-m2883	91.3 ± 6.9	104.2 ± 3.6
EGFR-m3154	52 ± 14.3	50.7 ± 9
EGFR-m3155	59 ± 7.6	52 ± 8
EGFR-m3156	77.8 ± 5.7	94.9 ± 3.7
EGFR-m3157	61.3 ± 5.1	49.2 ± 3.3
EGFR-m3158	55.5 ± 8	52.5 ± 5.6
EGFR-m3159	50.1 ± 3.7	41.3 ± 5.8

EGFR-m3160	78.1 ± 2.7	84.4 ± 3
EGFR-m3161	83.5 ± 7.3	94.6 ± 7.4
EGFR-m3162	82.8 ± 9.4	86.3 ± 5
EGFR-m3163	87.8 ± 1.4	101.5 ± 3.2
EGFR-m3166	83.3 ± 6	91.1 ± 1.9
EGFR-m3168	60.8 ± 4.2	62.5 ± 3
EGFR-m3474	33.5 ± 8.2	28.9 ± 7.6
EGFR-m3475	83.2 ± 6.8	91.2 ± 4.1
EGFR-m3491	55.6 ± 5.9	44.2 ± 6.1
EGFR-m3492	90.3 ± 2	54.9 ± 1.4
EGFR-m3493	73.8 ± 5.8	84.1 ± 6.2
EGFR-m3494	88.5 ± 4.3	73.2 ± 3.4
EGFR-m3495	76.1 ± 6.5	109.7 ± 1.6
EGFR-m3496	93.1 ± 7.5	108.2 ± 6.9
EGFR-m3497	96.9 ± 7.1	98.1 ± 6.3
EGFR-m4056	66.5 ± 10.1	44.8 ± 7.9
EGFR-m4103	63.7 ± 5.8	47.7 ± 5.8
EGFR-m4104	59 ± 5	60.7 ± 2.5
EGFR-m4105	71.4 ± 2	54.3 ± 5
EGFR-m4106	41.9 ± 12.5	34.1 ± 22.9
EGFR-m4109	49.8 ± N/A	112 ± 25
EGFR-m4309	72.2 ± 7.4	64.7 ± 9.4
EGFR-m4619	45.4 ± 6.6	27.8 ± 4.2
EGFR-m4627	63.2 ± 9.6	42 ± 11.3
EGFR-m5006	88.5 ± 4	82 ± 5.4
EGFR-m5007	81.8 ± 3.8	69.7 ± 4
EGFR-m5008	180.4 ± 9.2	167.4 ± 13.4
EGFR-m5012	56.4 ± 14.5	57.3 ± 3.3
EGFR-m5329	56 ± 5.3	68.9 ± 18.6
EGFR-m5330	62.3 ± 2.9	59 ± 2.2
EGFR-m5403	49.3 ± 4.8	35 ± 3.6
EGFR-m5638	81.8 ± 5.6	87.9 ± 4.7
EGFR-m5895	49.8 ± 7	38.9 ± 0.7

The following DsiRNAs were observed to reduce EGFR levels by 65% or more when administered to mouse cells (here, Hepa1-6 cells) at 1nM: EGFR-2462, EGFR-3089 and EGFR-m3474.

Assay results of Tables 11 and 12 above were also plotted and are shown in Figures 2A-2D.

In certain embodiments, double stranded nucleic acids were selected that target the following 21 nucleotide target sequences:

Table 13: EGFR 21 Nucleotide Target Sequences of Select dsRNAs

Human EGFR Target Location	21 Nucleotide Target Sequence	SEQ ID NO:
EGFR-390	CAGTTGGGCACTTTTGAAGAT	1431
EGFR-458	TGGGAATTTGGAAATTACCTA	1432
EGFR-464	TTTGGAAATTACCTATGTGCA	1550
EGFR-525	GTGGCTGGTTATGTCCTCATT	1434
EGFR-676	TGCCCATGAGAAATTTACAGG	1435
EGFR-707	TGGCGCCGTGCGGTTTCAGCAA	1437
EGFR-827	CAGCTGCCAAAAGTGTGATCC	1441
EGFR-876	GCAGGAGAGGAGAAGTGCCAG	1570
EGFR-877	CAGGAGAGGAGAAGTGCCAGA	1571
EGFR-878	AGGAGAGGAGAAGTGCCAGAA	1572
EGFR-1271	CCGCAAAGTGTGTAACGGAAT	1448
EGFR-1286	CGGAATAGGTATTGGTGAATT	1449
EGFR-1313	CTCACTCTCCATAAATGCTAC	1584
EGFR-1330	CTACGAATATTAAACACTTCA	1450
EGFR-1562	CAAGCAACATGGTCAGTTTTTC	1594
EGFR-1563	AAGCAACATGGTCAGTTTTTCT	1595
EGFR-1679	GTGCTATGCAAATACAATAAA	1454
EGFR-1723	CCGGTCAGAAAACCAAATTA	1455
EGFR-2011	TCCAGTGTGCCCACTACATTG	1602
EGFR-2458	GACTCTGGATCCCAGAAGGTG	1606
EGFR-2460	CTCTGGATCCCAGAAGGTGAG	1608
EGFR-2461	TCTGGATCCCAGAAGGTGAGA	1609
EGFR-2462	CTGGATCCCAGAAGGTGAGAA	1610
EGFR-2463	TGGATCCCAGAAGGTGAGAAA	1611
EGFR-2464	GGATCCCAGAAGGTGAGAAAG	1612
EGFR-2465	GATCCCAGAAGGTGAGAAAGT	1613
EGFR-2624	CACCGTGCAGCTCATCACGCA	1472
EGFR-2816	GCAGCATGTCAAGATCACAGA	1615
EGFR-2817	CAGCATGTCAAGATCACAGAT	1616
EGFR-2818	AGCATGTCAAGATCACAGATT	1617
EGFR-2819	GCATGTCAAGATCACAGATTT	1618
EGFR-2897	AGTGCCTATCAAGTGGATGGC	1643
EGFR-2915	GGCATTGGAATCAATTTTACA	1487
EGFR-3088	GTACCATCGATGTCTACATGA	1644
EGFR-3090	ACCATCGATGTCTACATGATC	1646

EGFR-3092	CATCGATGTCTACATGATCAT	1648
EGFR-3094	TCGATGTCTACATGATCATGG	1650
EGFR-3095	CGATGTCTACATGATCATGGT	1651
EGFR-3102	TACATGATCATGGTCAAGTGC	1658
EGFR-3103	ACATGATCATGGTCAAGTGCT	1659
EGFR-3105	ATGATCATGGTCAAGTGCTGG	1661
EGFR-3106	TGATCATGGTCAAGTGCTGGA	1662
EGFR-3107	GATCATGGTCAAGTGCTGGAT	1663
EGFR-3108	ATCATGGTCAAGTGCTGGATG	1664
EGFR-3109	TCATGGTCAAGTGCTGGATGA	1665
EGFR-3110	CATGGTCAAGTGCTGGATGAT	1666
EGFR-3111	ATGGTCAAGTGCTGGATGATA	1667
EGFR-3112	TGGTCAAGTGCTGGATGATAG	1668
EGFR-3115	TCAAGTGCTGGATGATAGACG	1488
EGFR-3117	AAGTGCTGGATGATAGACGCA	1489
EGFR-3118	AGTGCTGGATGATAGACGCAG	1490
EGFR-3120	TGCTGGATGATAGACGCAGAT	1491
EGFR-3222	GATGAAAGAATGCATTTGCCA	1674
EGFR-3223	ATGAAAGAATGCATTTGCCAA	1675
EGFR-3224	TGAAAGAATGCATTTGCCAAG	1676
EGFR-3372	CTCCTGAGCTCTCTGAGTGCA	1492
EGFR-3375	CTGAGCTCTCTGAGTGCAACC	1493
EGFR-3459	GACAGCTTCTTGCAGCGATAC	1498
EGFR-3772	TGGACAACCCTGACTACCAGC	1677
EGFR-3775	ACAACCCTGACTACCAGCAGG	1680
EGFR-3776	CAACCCTGACTACCAGCAGGA	1681
EGFR-3777	AACCCTGACTACCAGCAGGAC	1682
EGFR-3778	ACCCTGACTACCAGCAGGACT	1683
EGFR-3779	CCCTGACTACCAGCAGGACTT	1684
EGFR-3876	CCACAAAGCAGTGAATTTATT	1502
EGFR-4249	CGCTATTGATTTTTTACTTCAA	1505
EGFR-4455	GCCGGATCGGTACTGTATCAA	1520
EGFR-4550	TCCTTAGACTTACTTTTGTA	1521
EGFR-4806	TAAGGATAGCACCGCTTTTGT	1524
EGFR-4811	ATAGCACCGCTTTTGTTCCTCG	1529
EGFR-4816	ACCGCTTTTGTTCCTCGCAAAA	1532
EGFR-4817	CCGCTTTTGTTCCTCGCAAAA	1533
EGFR-4819	GCTTTTGTTCCTCGCAAAAACG	1535
EGFR-4953	CAAAATTAGTTTGTGTTACTT	1537
EGFR-5206	AAACTAGGGTTTGAAATTGAT	1540
EGFR-5506	TGTTCCTTTTGCTTTTAAAGT	1546

In further preferred embodiments, double stranded nucleic acids were selected that target the following 21 nucleotide target sequences:

Table 14: EGFR 21 Nucleotide Target Sequences of Further Selected dsRNAs

Human EGFR Target Location	21 Nucleotide Target Sequence	SEQ ID NO:
EGFR-390	CAGTTGGGCACTTTTGAAGAT	1431
EGFR-458	TGGGAATTTGGAAATTACCTA	1432
EGFR-877	CAGGAGAGGAGAAGTCCAGA	1571
EGFR-1271	CCGCAAAGTGTGTAACGGAAT	1448
EGFR-1313	CTCACTCTCCATAAATGCTAC	1584
EGFR-1330	CTACGAATATTAAACACTTCA	1450
EGFR-1563	AAGCAACATGGTCAGTTTTCT	1595
EGFR-1679	GTGCTATGCAAATACAATAAA	1454
EGFR-2460	CTCTGGATCCCAGAAGGTGAG	1608
EGFR-2462	CTGGATCCCAGAAGGTGAGAA	1610
EGFR-2463	TGGATCCCAGAAGGTGAGAAA	1611
EGFR-2465	GATCCCAGAAGGTGAGAAAGT	1613
EGFR-2915	GGCATTGGAATCAATTTTACA	1487
EGFR-3092	CATCGATGTCTACATGATCAT	1648
EGFR-3094	TCGATGTCTACATGATCATGG	1650
EGFR-3105	ATGATCATGGTCAAGTGCTGG	1661
EGFR-3108	ATCATGGTCAAGTGCTGGATG	1664
EGFR-3110	CATGGTCAAGTGCTGGATGAT	1666
EGFR-3111	ATGGTCAAGTGCTGGATGATA	1667
EGFR-3112	TGGTCAAGTGCTGGATGATAG	1668
EGFR-3118	AGTGCTGGATGATAGACGCAG	1490
EGFR-3222	GATGAAAGAATGCATTTGCCA	1674
EGFR-3223	ATGAAAGAATGCATTTGCCAA	1675
EGFR-3775	ACAACCCTGACTACCAGCAGG	1680
EGFR-3777	AACCCTGACTACCAGCAGGAC	1682
EGFR-4550	TCCTTAGACTTACTTTTGTA	1521

Example 3: DsiRNA Inhibition of EGFR – Secondary Screen

72 asymmetric DsiRNAs of the above experiment were then examined in a secondary assay (“Phase 2”), with results of such assays presented in histogram form in Figures 3A-3D. Specifically, the 72 asymmetric DsiRNAs selected from the 356 tested above were assessed for inhibition of human EGFR at 1 nM, 0.3 nM and 0.1 nM in the environment of human HeLa cells (Figures 3A-3B). These 72 asymmetric DsiRNAs were also assessed for

inhibition of mouse EGFR at 1 nM, 0.3 nM and 0.1 nM in the environment of mouse HEPA1-6 cells (Figures 3C-3D). As shown in Figures 3A-3B, a number of asymmetric DsiRNAs reproducibly exhibited robust human EGFR inhibitory efficacies at sub-nanomolar concentrations when assayed in the environment of HeLa cells. For example, the following DsiRNAs reproducibly exhibited greater than 70% reduction of EGFR levels when administered to mammalian cells (here, HeLa cells) at a concentration of 100pM or less in the environment of these cells: EGFR-390, EGFR-458, EGFR-4249, EGFR-4813 and EGFR-4953. In addition, as shown in Figures 3C-3D, a number of asymmetric DsiRNAs also showed significant mouse EGFR inhibitory efficacies at 1 nM, 300 pM and 100 pM when assayed in the environment of mouse HEPA1-6 cells. (Meanwhile, human EGFR-specific inhibitory asymmetric DsiRNAs were also identified.)

In certain preferred embodiments, DsiRNAs are selected from the following: EGFR-2915, EGFR-4249, EGFR-4550, EGFR-4811, EGFR-4812, EGFR-4813, EGFR-4817, EGFR-4970 and EGFR-5206. In such embodiments, the following 21 nucleotide sequences are targeted:

Table 15: EGFR 21 Nucleotide Target Sequences of Additional Selected dsRNAs

Human EGFR Target Location	21 Nucleotide Target Sequence	SEQ ID NO:
EGFR-2915	GGCATTGGAATCAATTTTACA	1487
EGFR-4249	CGCTATTGATTTTACTTCAA	1505
EGFR-4550	TCCTTAGACTTACTTTTGTA	1521
EGFR-4811	ATAGCACCGCTTTTGTTCTCG	1529
EGFR-4812	TAGCACCGCTTTTGTTCTCGC	1530
EGFR-4813	AGCACCGCTTTTGTTCTCGCA	1531
EGFR-4817	CCGCTTTTGTTCTCGCAAAAA	1533
EGFR-4970	ACTTATGGAAGATAGTTTCT	1538
EGFR-5206	AAACTAGGGTTTGAAATTGAT	1540

In further embodiments, other selections of duplexes and corresponding EGFR mRNA targets are made, with such further selections of target sequences shown in Tables 16-26.

Table 16: Further EGFR mRNA Target Sequences of dsRNAs

**Human EGFR
Duplex**

Target mRNA Sequence

SEQ ID NO:

EGFR-390	CAGUUGGGCACUUUUGAAGAUCAUUUU	2143
EGFR-390	CAGUUGGGCACUUUUGAAGAU	2515
EGFR-390	CAGUUGGGCACUUUUGAAG	3295
EGFR-390	AGUUGGGCACUUUUGAAGA	3035
EGFR-390	GUUGGGCACUUUUGAAGAU	2775
EGFR-458	UGGGAAUUUGGAAAUUACCUAUGUGCA	2144
EGFR-458	UGGGAAUUUGGAAAUUACCUA	2516
EGFR-458	UGGGAAUUUGGAAAUUACC	3296
EGFR-458	GGGAAUUUGGAAAUUACCU	3036
EGFR-458	GGAAUUUGGAAAUUACCUA	2776
EGFR-878	AGGAGAGGAGAACUGCCAGAAACUGAC	2284
EGFR-878	AGGAGAGGAGAACUGCCAGAA	2656
EGFR-878	AGGAGAGGAGAACUGCCAG	3436
EGFR-878	GGAGAGGAGAACUGCCAGA	3176
EGFR-878	GAGAGGAGAACUGCCAGAA	2916
EGFR-1271	CCGCAAAGUGUGUAACGGAAUAGGU AU	2160
EGFR-1271	CCGCAAAGUGUGUAACGGAAU	2532
EGFR-1271	CCGCAAAGUGUGUAACGG A	3312
EGFR-1271	CGCAAAGUGUGUAACGGAA	3052
EGFR-1271	GCAAAGUGUGUAACGGAAU	2792
EGFR-1286	CGGAAUAGGU AUUGGUGAAUUUAAAGA	2161
EGFR-1286	CGGAAUAGGU AUUGGUGAAUU	2533
EGFR-1286	CGGAAUAGGU AUUGGUGAA	3313
EGFR-1286	GGAAUAGGU AUUGGUGAAU	3053
EGFR-1286	GAAUAGGU AUUGGUGAAUU	2793
EGFR-1313	CUCACUCUCCA UAAAUGCUACGAAU AU	2296
EGFR-1313	CUCACUCUCCA UAAAUGCUAC	2668
EGFR-1313	CUCACUCUCCA UAAAUGCU	3448
EGFR-1313	UCACUCUCCA UAAAUGCUA	3188
EGFR-1313	CACUCUCCA UAAAUGCUAC	2928
EGFR-1330	CUACGAAU AUUAAACACUUCAAAAACU	2162
EGFR-1330	CUACGAAU AUUAAACACUUC A	2534
EGFR-1330	CUACGAAU AUUAAACACUU	3314
EGFR-1330	UACGAAU AUUAAACACUUC	3054
EGFR-1330	ACGAAU AUUAAACACUUC A	2794
EGFR-1563	AAGCAACAUGGUCAGUUUUCUCUUGCA	2307
EGFR-1563	AAGCAACAUGGUCAGUUUUCU	2679
EGFR-1563	AAGCAACAUGGUCAGUUUU	3459
EGFR-1563	AGCAACAUGGUCAGUUUUC	3199
EGFR-1563	GCAACAUGGUCAGUUUUCU	2939
EGFR-1679	GUGCUAUGCAAAUACAAUAAACUGGAA	2166

EGFR-1679	GUGCUAUGCAAAUACAAUAAA	2538
EGFR-1679	GUGCUAUGCAAAUACAAUA	3318
EGFR-1679	UGCUAUGCAAAUACAAUAA	3058
EGFR-1679	GCUAUGCAAAUACAAUAAA	2798
EGFR-2458	GACUCUGGAUCCCAGAAGGUGAGAAAAG	2318
EGFR-2458	GACUCUGGAUCCCAGAAGGUG	2690
EGFR-2458	GACUCUGGAUCCCAGAAGG	3470
EGFR-2458	ACUCUGGAUCCCAGAAGGU	3210
EGFR-2458	CUCUGGAUCCCAGAAGGUG	2950
EGFR-2462	CUGGAUCCCAGAAGGUGAGAAAGUUAA	2322
EGFR-2462	CUGGAUCCCAGAAGGUGAGAA	2694
EGFR-2462	CUGGAUCCCAGAAGGUGAG	3474
EGFR-2462	UGGAUCCCAGAAGGUGAGA	3214
EGFR-2462	GGAUCCCAGAAGGUGAGAA	2954
EGFR-2464	GGAUCCCAGAAGGUGAGAAAGUUAAAA	2324
EGFR-2464	GGAUCCCAGAAGGUGAGAAAG	2696
EGFR-2464	GGAUCCCAGAAGGUGAGAA	3476
EGFR-2464	GAUCCCAGAAGGUGAGAAA	3216
EGFR-2464	AUCCCAGAAGGUGAGAAAG	2956
EGFR-2915	GGCAUUGGAAUCAAUUUUACACAGAAU	2199
EGFR-2915	GGCAUUGGAAUCAAUUUUACA	2571
EGFR-2915	GGCAUUGGAAUCAAUUUUA	3351
EGFR-2915	GCAUUGGAAUCAAUUUUAC	3091
EGFR-2915	CAUUGGAAUCAAUUUUACA	2831
EGFR-3111	AUGGUCAAGUGCUGGAUGAUAGACGCA	2379
EGFR-3111	AUGGUCAAGUGCUGGAUGAUA	2751
EGFR-3111	AUGGUCAAGUGCUGGAUGA	3531
EGFR-3111	UGGUCAAGUGCUGGAUGAU	3271
EGFR-3111	GGUCAAGUGCUGGAUGAUA	3011
EGFR-3112	UGGUCAAGUGCUGGAUGAUAGACGCAG	2380
EGFR-3112	UGGUCAAGUGCUGGAUGAUAG	2752
EGFR-3112	UGGUCAAGUGCUGGAUGAU	3532
EGFR-3112	GGUCAAGUGCUGGAUGAUA	3272
EGFR-3112	GUCAAGUGCUGGAUGAUAG	3012
EGFR-3223	AUGAAAGAAUGCAUUUGCCAAGUCCUA	2387
EGFR-3223	AUGAAAGAAUGCAUUUGCCAA	2759
EGFR-3223	AUGAAAGAAUGCAUUUGCC	3539
EGFR-3223	UGAAAGAAUGCAUUUGCCA	3279
EGFR-3223	GAAAGAAUGCAUUUGCCAA	3019
EGFR-4249	CGCUAUUGAUUUUUACUUCAAUGGGCU	2217
EGFR-4249	CGCUAUUGAUUUUUACUUCAA	2589
EGFR-4249	CGCUAUUGAUUUUUACUUC	3369
EGFR-4249	GCUAUUGAUUUUUACUUCA	3109

EGFR-4249	CUAUUGAUUUUUACUUCAA	2849
EGFR-4450	AGCAGGCCGGAUCGGUACUGUAUCAAG	2231
EGFR-4450	AGCAGGCCGGAUCGGUACUGU	2603
EGFR-4450	AGCAGGCCGGAUCGGUACU	3383
EGFR-4450	GCAGGCCGGAUCGGUACUG	3123
EGFR-4450	CAGGCCGGAUCGGUACUGU	2863
EGFR-4455	GCCGGAUCGGUACUGUAUCAAGUCAUG	2232
EGFR-4455	GCCGGAUCGGUACUGUAUCAA	2604
EGFR-4455	GCCGGAUCGGUACUGUAUC	3384
EGFR-4455	CCGGAUCGGUACUGUAUCA	3124
EGFR-4455	CGGAUCGGUACUGUAUCAA	2864
EGFR-4550	UCCUUAGACUUACUUUUGUAAAAAUGU	2233
EGFR-4550	UCCUUAGACUUACUUUUGUAA	2605
EGFR-4550	UCCUUAGACUUACUUUUGU	3385
EGFR-4550	CCUUAGACUUACUUUUGUA	3125
EGFR-4550	CUUAGACUUACUUUUGUAA	2865
EGFR-4806	UAAGGAUAGCACCGCUUUUGUUCUCGC	2236
EGFR-4806	UAAGGAUAGCACCGCUUUUGU	2608
EGFR-4806	UAAGGAUAGCACCGCUUUU	3388
EGFR-4806	AAGGAUAGCACCGCUUUUG	3128
EGFR-4806	AGGAUAGCACCGCUUUUGU	2868
EGFR-4809	GGAUAGCACCGCUUUUGUUCUCGCAAA	2239
EGFR-4809	GGAUAGCACCGCUUUUGUUCU	2611
EGFR-4809	GGAUAGCACCGCUUUUGUU	3391
EGFR-4809	GAUAGCACCGCUUUUGUUC	3131
EGFR-4809	AUAGCACCGCUUUUGUUCU	2871
EGFR-4811	AUAGCACCGCUUUUGUUCUCGCAAAAA	2241
EGFR-4811	AUAGCACCGCUUUUGUUCUCG	2613
EGFR-4811	AUAGCACCGCUUUUGUUCU	3393
EGFR-4811	UAGCACCGCUUUUGUUCUC	3133
EGFR-4811	AGCACCGCUUUUGUUCUCG	2873
EGFR-4812	UAGCACCGCUUUUGUUCUCGCAAAAAC	2242
EGFR-4812	UAGCACCGCUUUUGUUCUCGC	2614
EGFR-4812	UAGCACCGCUUUUGUUCUC	3394
EGFR-4812	AGCACCGCUUUUGUUCUCG	3134
EGFR-4812	GCACCGCUUUUGUUCUCGC	2874
EGFR-4813	AGCACCGCUUUUGUUCUCGCAAAAACG	2243
EGFR-4813	AGCACCGCUUUUGUUCUCGCA	2615
EGFR-4813	AGCACCGCUUUUGUUCUCG	3395
EGFR-4813	GCACCGCUUUUGUUCUCGC	3135
EGFR-4813	CACCGCUUUUGUUCUCGCA	2875
EGFR-4817	CCGCUUUUGUUCUCGCAAAAACGUAUC	2245
EGFR-4817	CCGCUUUUGUUCUCGCAAAAA	2617

EGFR-4817	CCGCUUUUGUUCUCGCAAA	3397
EGFR-4817	CGCUUUUGUUCUCGCAAAA	3137
EGFR-4817	GCUUUUGUUCUCGCAAAAA	2877
EGFR-4819	GCUUUUGUUCUCGCAAAAACGUAUCUC	2247
EGFR-4819	GCUUUUGUUCUCGCAAAAACG	2619
EGFR-4819	GCUUUUGUUCUCGCAAAAA	3399
EGFR-4819	CUUUUGUUCUCGCAAAAAC	3139
EGFR-4819	UUUUGUUCUCGCAAAAACG	2879
EGFR-4953	CAAAAUUAGUUUGUGUUACUUAUGGAA	2249
EGFR-4953	CAAAAUUAGUUUGUGUUACUU	2621
EGFR-4953	CAAAAUUAGUUUGUGUUAC	3401
EGFR-4953	AAAUUAGUUUGUGUUACU	3141
EGFR-4953	AAAUUAGUUUGUGUUACUU	2881
EGFR-4970	ACUUAUGGAAGAUAGUUUUCUCCUUUU	2250
EGFR-4970	ACUUAUGGAAGAUAGUUUUCU	2622
EGFR-4970	ACUUAUGGAAGAUAGUUUU	3402
EGFR-4970	CUUAUGGAAGAUAGUUUUC	3142
EGFR-4970	UUAUGGAAGAUAGUUUUCU	2882
EGFR-5003	CUUCAAAAGCUUUUUACUCAAGAGUA	2251
EGFR-5003	CUUCAAAAGCUUUUUACUCAA	2623
EGFR-5003	CUUCAAAAGCUUUUUACUC	3403
EGFR-5003	UUCAAAAGCUUUUUACUCA	3143
EGFR-5003	UCAAAAGCUUUUUACUCAA	2883
EGFR-5206	AAACUAGGGUUUGAAAUUGAUAUUGCU	2252
EGFR-5206	AAACUAGGGUUUGAAAUUGAU	2624
EGFR-5206	AAACUAGGGUUUGAAAUUG	3404
EGFR-5206	AACUAGGGUUUGAAAUUGA	3144
EGFR-5206	ACUAGGGUUUGAAAUUGAU	2884

Table 17: Select EGFR mRNA Target Sequences of dsRNAs

Human EGFR Duplex	Target mRNA Sequence	SEQ ID NO:
EGFR-2915	GGCAUUGGAAUCAAUUUUACACAGAAU	2199
EGFR-2915	GGCAUUGGAAUCAAUUUUACA	2571
EGFR-2915	GGCAUUGGAAUCAAUUUUA	3351
EGFR-2915	GCAUUGGAAUCAAUUUUAC	3091
EGFR-2915	CAUUGGAAUCAAUUUUACA	2831
EGFR-4455	GCCGGAUCGGUACUGUAUCAAGUCAUG	2232
EGFR-4455	GCCGGAUCGGUACUGUAUCAA	2604
EGFR-4455	GCCGGAUCGGUACUGUAUC	3384
EGFR-4455	CCGGAUCGGUACUGUAUCA	3124
EGFR-4455	CGGAUCGGUACUGUAUCAA	2864
EGFR-4550	UCCUUAGACUUACUUUUGUAAAAAUGU	2233

EGFR-4550	UCCUUAGACUUACUUUUGUAA	2605
EGFR-4550	UCCUUAGACUUACUUUUGU	3385
EGFR-4550	CCUUAGACUUACUUUUGUA	3125
EGFR-4550	CUUAGACUUACUUUUGUAA	2865
EGFR-4813	AGCACCGCUUUUGUUCUCGCAAAAACG	2243
EGFR-4813	AGCACCGCUUUUGUUCUCGCA	2615
EGFR-4813	AGCACCGCUUUUGUUCUCG	3395
EGFR-4813	GCACCGCUUUUGUUCUCGC	3135
EGFR-4813	CACCGCUUUUGUUCUCGCA	2875
EGFR-5003	CUUCAAAAGCUUUUUACUCAAGAGUA	2251
EGFR-5003	CUUCAAAAGCUUUUUACUCAA	2623
EGFR-5003	CUUCAAAAGCUUUUUACUC	3403
EGFR-5003	UUCAAAAGCUUUUUACUCA	3143
EGFR-5003	UCAAAAGCUUUUUACUCAA	2883

Table 18: Additional Select EGFR mRNA Target Sequences of dsRNAs

Human EGFR Duplex	Target mRNA Sequence	SEQ ID NO:
EGFR-1330	CUACGAAUAUUAACACUCAAACU	2162
EGFR-1330	CUACGAAUAUUAACACUUA	2534
EGFR-1330	CUACGAAUAUUAACACUU	3314
EGFR-1330	UACGAAUAUUAACACUUC	3054
EGFR-1330	ACGAAUAUUAACACUUA	2794
EGFR-4450	AGCAGGCCGGAUCGGUACUGUAUCAAG	2231
EGFR-4450	AGCAGGCCGGAUCGGUACUGU	2603
EGFR-4450	AGCAGGCCGGAUCGGUACU	3383
EGFR-4450	GCAGGCCGGAUCGGUACUG	3123
EGFR-4450	CAGGCCGGAUCGGUACUGU	2863
EGFR-4811	AUAGCACCGCUUUUGUUCUCGCAAAAA	2241
EGFR-4811	AUAGCACCGCUUUUGUUCUCG	2613
EGFR-4811	AUAGCACCGCUUUUGUUCU	3393
EGFR-4811	UAGCACCGCUUUUGUUCUC	3133
EGFR-4811	AGCACCGCUUUUGUUCUCG	2873
EGFR-4812	UAGCACCGCUUUUGUUCUCGCAAAAAC	2242
EGFR-4812	UAGCACCGCUUUUGUUCUCGC	2614
EGFR-4812	UAGCACCGCUUUUGUUCUC	3394
EGFR-4812	AGCACCGCUUUUGUUCUCG	3134
EGFR-4812	GCACCGCUUUUGUUCUCGC	2874
EGFR-4817	CCGCUUUUGUUCUCGCAAAAACGUAUC	2245
EGFR-4817	CCGCUUUUGUUCUCGCAAAAA	2617
EGFR-4817	CCGCUUUUGUUCUCGCAAA	3397
EGFR-4817	CGCUUUUGUUCUCGCAAAA	3137
EGFR-4817	GCUUUUGUUCUCGCAAAAA	2877

Table 19: Further Select EGFR mRNA Target Sequences of dsRNAs

Human EGFR Duplex	Target mRNA Sequence	SEQ ID NO:
EGFR-878	AGGAGAGGAGAACUGCCAGAAACUGAC	2284
EGFR-878	AGGAGAGGAGAACUGCCAGAA	2656
EGFR-878	AGGAGAGGAGAACUGCCAG	3436
EGFR-878	GGAGAGGAGAACUGCCAGA	3176
EGFR-878	GAGAGGAGAACUGCCAGAA	2916
EGFR-1286	CGGAAUAGGUAAUUGGUGAAUUUAAAGA	2161
EGFR-1286	CGGAAUAGGUAAUUGGUGAAUU	2533
EGFR-1286	CGGAAUAGGUAAUUGGUGAA	3313
EGFR-1286	GGAAUAGGUAAUUGGUGAAU	3053
EGFR-1286	GAAUAGGUAAUUGGUGAAUU	2793
EGFR-1679	GUGCUAUGCAAAUACAAUAAACUGGAA	2166
EGFR-1679	GUGCUAUGCAAAUACAAUAAA	2538
EGFR-1679	GUGCUAUGCAAAUACAAUA	3318
EGFR-1679	UGCUAUGCAAAUACAAUAA	3058
EGFR-1679	GCUAUGCAAAUACAAUAAA	2798
EGFR-4249	CGCUAUUGAUUUUUACUUCAAUGGGCU	2217
EGFR-4249	CGCUAUUGAUUUUUACUUCAA	2589
EGFR-4249	CGCUAUUGAUUUUUACUUC	3369
EGFR-4249	GCUAUUGAUUUUUACUUCA	3109
EGFR-4249	CUAUUGAUUUUUACUUCAA	2849
EGFR-4819	GCUUUUGUUCUCGCAAAAACGUAUCUC	2247
EGFR-4819	GCUUUUGUUCUCGCAAAAACG	2619
EGFR-4819	GCUUUUGUUCUCGCAAAAA	3399
EGFR-4819	CUUUUGUUCUCGCAAAAAC	3139
EGFR-4819	UUUUGUUCUCGCAAAAACG	2879
EGFR-5206	AAACUAGGGUUUGAAAUUGAUAAUGCU	2252
EGFR-5206	AAACUAGGGUUUGAAAUUGAU	2624
EGFR-5206	AAACUAGGGUUUGAAAUUG	3404
EGFR-5206	AACUAGGGUUUGAAAUUGA	3144
EGFR-5206	ACUAGGGUUUGAAAUUGAU	2884

Table 20: Additional Selected EGFR mRNA Target Sequences of dsRNAs

Human EGFR Duplex	Target mRNA Sequence	SEQ ID NO:
EGFR-390	CAGUUGGGCACUUUUGAAGAUCAUUUU	2143
EGFR-1271	CCGCAAAGUGUGUAACGGAAUAGGUAU	2160
EGFR-1563	AAGCAACAUGGUCAGUUUUCUCUUGCA	2307
EGFR-2462	CUGGAUCCCAGAAGGUGAGAAAGUUAA	2322
EGFR-2464	GGAUCCCAGAAGGUGAGAAAGUUAAAA	2324

EGFR-3111	AUGGUCAAGUGCUGGAUGAUAGACGCA	2379
EGFR-3112	UGGUCAAGUGCUGGAUGAUAGACGCAG	2380
EGFR-3223	AUGAAAGAAUGCAUUUGCCAAGUCCUA	2387
EGFR-4806	UAAGGAUAGCACCGCUUUUGUUCUCGC	2236

Table 21: More Selected EGFR mRNA Target Sequences of dsRNAs

Human EGFR Duplex	Target mRNA Sequence	SEQ ID NO:
EGFR-458	UGGGAAUUUGGAAAUUACCUAUGUGCA	2144
EGFR-458	UGGGAAUUUGGAAAUUACCUA	2516
EGFR-458	UGGGAAUUUGGAAAUUACC	3296
EGFR-4970	ACUUAUGGAAGAUAGUUUUCUCCUUUU	2250
EGFR-4970	ACUUAUGGAAGAUAGUUUUCU	2622
EGFR-4970	ACUUAUGGAAGAUAGUUUU	3402

Table 22: Further Selected EGFR mRNA Target Sequences of dsRNAs

Human EGFR Duplex	Target mRNA Sequence	SEQ ID NO:
EGFR-4809	GGAUAGCACCGCUUUUGUUCUCGCAAA	2239
EGFR-4809	GGAUAGCACCGCUUUUGUUCU	2611
EGFR-4809	GAUAGCACCGCUUUUGUUC	3131
EGFR-4809	AUAGCACCGCUUUUGUUCU	2871
EGFR-4953	CAAAAUUAGUUUGUGUUACUUAUGGAA	2249
EGFR-4953	CAAAAUUAGUUUGUGUUACUU	2621
EGFR-4953	AAAUUAGUUUGUGUUACU	3141
EGFR-4953	AAAUUAGUUUGUGUUACUU	2881

Table 23: Additional EGFR mRNA Target Sequences of dsRNAs

Human EGFR Duplex	Target mRNA Sequence	SEQ ID NO:
EGFR-1313	CUCACUCUCCAUAUAAUGCUACGAAUUAU	2296
EGFR-1313	CUCACUCUCCAUAUAAUGCUAC	2668
EGFR-1313	CUCACUCUCCAUAUAAUGCU	3448
EGFR-1313	UCACUCUCCAUAUAAUGCUA	3188
EGFR-2458	GACUCUGGAUCCCAGAAGGUGAGAAAG	2318
EGFR-2458	GACUCUGGAUCCCAGAAGGUG	2690
EGFR-2458	GACUCUGGAUCCCAGAAGG	3470
EGFR-2458	ACUCUGGAUCCCAGAAGGU	3210

Table 24: More EGFR mRNA Target Sequences of dsRNAs

Human EGFR Duplex	Target mRNA Sequence	SEQ ID NO:
EGFR-390	CAGUUGGGCACUUUUGAAGAU	2515
EGFR-390	CAGUUGGGCACUUUUGAAG	3295
EGFR-390	AGUUGGGCACUUUUGAAGA	3035
EGFR-390	GUUGGGCACUUUUGAAGAU	2775
EGFR-1563	AAGCAACAUGGUCAGUUUUCU	2679
EGFR-1563	AAGCAACAUGGUCAGUUUU	3459
EGFR-1563	AGCAACAUGGUCAGUUUUC	3199
EGFR-1563	GCAACAUGGUCAGUUUUCU	2939
EGFR-2462	CUGGAUCCCAGAAGGUGAGAA	2694
EGFR-2462	CUGGAUCCCAGAAGGUGAG	3474
EGFR-2462	UGGAUCCCAGAAGGUGAGA	3214
EGFR-2462	GGAUCCCAGAAGGUGAGAA	2954
EGFR-3111	AUGGUCAAGUGCUGGAUGAUA	2751
EGFR-3111	AUGGUCAAGUGCUGGAUGA	3531
EGFR-3111	UGGUCAAGUGCUGGAUGAU	3271
EGFR-3111	GGUCAAGUGCUGGAUGAUA	3011
EGFR-3112	UGGUCAAGUGCUGGAUGAUAG	2752
EGFR-3112	UGGUCAAGUGCUGGAUGAU	3532
EGFR-3112	GGUCAAGUGCUGGAUGAUA	3272
EGFR-3112	GUCAAGUGCUGGAUGAUAG	3012
EGFR-3223	AUGAAAGAAUGCAUUUGCCAA	2759
EGFR-3223	AUGAAAGAAUGCAUUUGCC	3539
EGFR-3223	UGAAAGAAUGCAUUUGCCA	3279
EGFR-3223	GAAAGAAUGCAUUUGCCAA	3019
EGFR-4806	UAAGGAUAGCACCGCUUUUGU	2608
EGFR-4806	UAAGGAUAGCACCGCUUUU	3388
EGFR-4806	AAGGAUAGCACCGCUUUUG	3128
EGFR-4806	AGGAUAGCACCGCUUUUGU	2868

Table 25: Additional mRNA Target Sequences of EGFR Inhibiting dsRNAs

Human EGFR Duplex	Target mRNA Sequence	SEQ ID NO:
EGFR-458	GGAAUUUGGAAAUUACCUA	2776
EGFR-4970	UUAUGGAAGAUAGUUUUCU	2882

Table 26: Further mRNA Target Sequences of EGFR Inhibiting dsRNAs

Human EGFR Duplex	Target mRNA Sequence	SEQ ID NO:
EGFR-4809	GGAUAGCACCGCUUUUGUU	3391
EGFR-4953	CAAAAUUAGUUUGUGUUAC	3401

Example 4: Modified Forms of EGFR-Targeting DsiRNAs Reduced EGFR Levels *In Vitro*

32 EGFR-targeting DsiRNAs (EGFR-878, EGFR-1313, EGFR-1563, EGFR-2458, EGFR-2462, EGFR-2464, EGFR-3111, EGFR-3112, EGFR-3223, EGFR-390, EGFR-458, EGFR-1271, EGFR-1286, EGFR-1330, EGFR-1679, EGFR-2915, EGFR-4249, EGFR-4450, EGFR-4455, EGFR-4550, EGFR-4806, EGFR-4809, EGFR-4811, EGFR-4812, EGFR-4813, EGFR-4817, EGFR-4819, EGFR-4953, EGFR-4970, EGFR-5003, EGFR-5206 and EGFR-m3474) were prepared with 2'-O-methyl modification patterns as shown in Figure 4A. For each of the 32 DsiRNA sequences, DsiRNAs possessing each of the six modification patterns were assayed for EGFR inhibition in human HeLa cells at 0.1 nM (in parallel assays) and 1.0 nM concentrations in the environment of the HeLa cells. Results of these experiments are presented as histograms in Figures 4B to 4I. In general, the 32 DsiRNA sequences exhibited a trend towards reduced efficacy of EGFR inhibition as the extent of 2'-O-methyl modification of the guide strand increased. However, for almost all DsiRNA sequences examined, a modification pattern could be identified that allowed the DsiRNA to retain significant EGFR inhibitory efficacy *in vitro*. It was also notable that many DsiRNAs (*e.g.*, EGFR-1286, EGFR-4249, EGFR-4550, EGFR-4806, EGFR-4813, EGFR-4817, EGFR-4819, EGFR-4953, EGFR-4970, EGFR-5003 and EGFR-5206) exhibited robust EGFR inhibitory efficacy in even the most highly modified states examined (*e.g.*, the M1 modification pattern). These data confirm that it is possible to identify effective DsiRNA sequences possessing high levels of modification, a trait advantageous for stabilizing such DsiRNAs and/or reducing immunogenicity of such DsiRNAs when therapeutically administered to a subject *in vivo*.

Example 5: Dose-Response of Selected EGFR-Targeting DsiRNAs

Six EGFR-targeting DsiRNAs were selected for assessment of dose-response characteristics *in vitro* in NCI-H1975 mammalian cells. The six duplexes assessed for dose-response were EGFR-390-M0/M35, EGFR-2915-M0/M35, EGFR-4806-M0/M35, EGFR-4806-M0/M25, EGFR-4249-M0/M25 and EGFR-4249-M0/M1 (where modifications of the duplexes are indicated as “passenger strand modification pattern/guide strand modification pattern”). As shown in Figure 5, sub-nanomolar IC₅₀ values were observed for all six such duplexes – indeed, single digit picomolar and even sub-picomolar IC₅₀ values were observed.

Thus, EGFR-targeting DsiRNAs were further demonstrated to be remarkably potent and effective inhibitors of EGFR expression.

Example 6: EGFR-Targeting DsiRNAs Selectively Inhibited NSCLC Cell Line Growth

In this Example, EGFR-targeting DsiRNAs EGFR-4249 M25 and EGFR-4806 M25 (note: modification pattern M25 was present on the guide strand of each of the preceding DsiRNAs) were examined for the ability to inhibit growth of tumor cell lines *in vitro*. Specifically, non-small cell lung cancer (NSCLC) cell lines NCI-H1975 (an erlotinib resistant NSCLC line), NCI-H292 (comprising a KRAS mutation), NCI-H460 (comprising a KRAS mutation) and A549 were examined for both EGFR mRNA knockdown and inhibition of cell growth following administration of EGFR-targeting DsiRNAs. As shown for NCI-H1975 in Figure 6, EGFR-targeting DsiRNAs EGFR-4249 M25 and EGFR-4806 M25 not only reduced expression levels of EGFR mRNA by 60% to 80% or more in NCI-H1975 cells, but also exhibited a dose-dependent inhibition of NCI-H1975 cell growth at tested 3 nM and 10 nM concentrations. Notably, the magnitude of NCI-H1975 cell growth inhibition was approximately 20% for cells administered either DsiRNA at 3 nM, while cell growth was inhibited by 40% to 50% when either DsiRNA was administered at 10 nM. The growth inhibition result observed for NCI-H1975 cells was particularly striking, in view of the lack of observation of such a growth inhibition effect in any of NCI-H292, NCI-H460 and A549 cells (data not shown; in each case, effective EGFR mRNA knockdown was confirmed, but no corresponding growth inhibition was observed). Accordingly, EGFR-targeting duplexes were observed to be effective inhibitors of tumor cell growth, at least in the instance of the erlotinib-resistant NCI-H1975 NSCLC cell line.

Example 7: EGFR-Targeting DsiRNAs Reduce EGFR Protein Levels *In Vitro*

The impact of an EGFR-targeting DsiRNA upon cellular protein levels is examined *in vitro*. Specifically, one of the above EGFR-targeting DsiRNAs possessing a 2'-O-methyl modification pattern as shown herein is delivered to human HeLa cells and is shown to dramatically reduce EGFR protein levels. In such experiments, DsiRNA transfection of HeLa cells can occur on day 0 at 10 nM concentration. On day 2, HeLa cells are harvested and cellular proteins are isolated for Western blot analysis. A Western blot is then probed with anti-EGFR antibody, with appropriate control protein levels assayed for purpose of

normalization of EGFR protein levels between samples. A non-specific, scrambled control DsiRNA can also be run in parallel for normalization purposes. Significant knockdown of EGFR protein levels is observed for the assayed DsiRNA and is seen to correlate with EGFR mRNA knockdown.

Example 8: Further DsiRNA Inhibition of EGFR

DsiRNA molecules selected from Table 2 above that target EGFR wild-type sequences are designed and synthesized as described above and tested in HeLa cells for inhibitory efficacy as described in Examples 1, 2, 3, 4, 5 or 6 above. The ability of these DsiRNA agents to inhibit EGFR expression is assessed in comparison to corresponding EGFR target sequence-directed 21mer siRNAs (tested anti-EGFR 21mer agents are designed with antisense strands complementary to the 21 nucleotide target sequences as shown in Table 6 above corresponding to tested DsiRNA agents; Figure 1 also presents a comparison of structures used in such experiments). Instances in which the DsiRNA of a DsiRNA-cognate siRNA pair outperforms the corresponding siRNA are identified (*e.g.*, at 24 hours post-administration, at concentrations of 0.1 nM). Such results demonstrate that DsiRNA activities do not directly correlate with siRNA activities, nor does the converse hold. Accordingly, such results demonstrate that DsiRNAs and siRNAs engage the RNA interference machinery differently, and that DsiRNAs and siRNAs – in spite of both comprising double-stranded RNA – are, in fact, different drugs.

Example 9: *In Vivo* Efficacy of EGFR-Targeting DsiRNAs in Targeted Tissues

To test the activity of a DsiRNA directed against EGFR *in vivo*, CD1 male mice are administered an EGFR-targeting DsiRNA. Mice are treated by i.v. tail vein injection with either 5% glucose (control vehicle), a control DsiRNA, or the EGFR-targeting DsiRNA. DsiRNAs are formulated in InVivoFectamineTM (Invitrogen) or other appropriate formulation, and are administered at a dose of, *e.g.*, 10mg/kg body weight per administration (administered on two days separated by one non-dosing day). Three days after the last administration, animals are sacrificed and tissues of interest (*e.g.*, lung, colon, liver, spleen, kidney, etc.) are harvested. For RNA expression analysis, RNA is isolated from tissue lysates using a PromegaTM SV96 RNA isolation kit. RNA is reverse-transcribed, and then Taqman quantitative PCR is performed on a BioRad CFX96, in multiplex using primer and probe sets

specific for EGFR and a housekeeping gene (*e.g.*, GAPDH) for normalization. The *in vivo* knockdown efficacy of EGFR in harvested tissues is thereby assessed and confirmed.

Example 10: Indications

The present body of knowledge in EGFR research indicates the need for methods to assay EGFR activity and for compounds that can regulate EGFR expression for research, diagnostic, and therapeutic use. As described herein, the nucleic acid molecules of the present invention can be used in assays to diagnose disease state related to EGFR levels. In addition, the nucleic acid molecules can be used to treat disease state related to EGFR misregulation, levels, etc.

Particular disorders and disease states that can be associated with EGFR expression modulation include, but are not limited to cancer and/or proliferative diseases, conditions, or disorders and other diseases, conditions or disorders that are related to or will respond to the levels of EGFR in a cell or tissue, alone or in combination with other therapies. Particular disease or disorder states that are associated with EGFR expression modulation include but are not limited to, for example, colorectal cancer, lung cancer, squamous cell carcinoma (*e.g.*, of the head and neck (SCCHN), renal cancer, breast cancer, bladder cancer, ovarian cancer, cervical cancer, esophageal cancer, gastric cancer, endometrial cancer, oropharyngeal cancer, and pancreatic cancer.

Gemcitabine and cyclophosphamide are non-limiting examples of chemotherapeutic agents that can be combined with or used in conjunction with the nucleic acid molecules (*e.g.* DsiRNA molecules) of the instant invention. Those skilled in the art will recognize that other drugs such as anti-cancer compounds and therapies can similarly be readily combined with the nucleic acid molecules of the instant invention (*e.g.* DsiRNA molecules) and are hence within the scope of the instant invention. Such compounds and therapies are well known in the art (see for example *Cancer: Principles and Practice of Oncology*, Volumes 1 and 2, eds Devita, V. T., Hellman, S., and Rosenberg, S. A., J.B. Lippincott Company, Philadelphia, USA) and include, without limitations, antifolates; fluoropyrimidines; cytarabine; purine analogs; adenosine analogs; amsacrine; topoisomerase I inhibitors; anthracyclins; retinoids; antibiotics such as bleomycin, anthracyclins, mitomycin C, dactinomycin, and mithramycin; hexamethylmelamine; dacarbazine; 1-asparaginase; platinum analogs; alkylating agents such as nitrogen mustard, melphalan, chlorambucil, busulfan, ifosfamide, 4-hydroperoxycyclophosphamide, nitrosoureas, thiopeta; plant derived compounds such as

vinca alkaloids, epipodophyllotoxins, taxol; Tamoxifen; radiation therapy; surgery; nutritional supplements; gene therapy; radiotherapy such as 3D-CRT; immunotoxin therapy such as ricin, monoclonal antibodies Herceptin; and the like.

For EGFR in particular, various monoclonal antibody and small molecule inhibitors that target EGFR have been described, and can be combined with the nucleic acids of the instant invention: such EGFR-targeting agents include, *e.g.*, cetuximab, panitumumab, zalutumumab, nimotuzumab, matuzumab, gefitinib, erlotinib and lapatinib (mixed EGFR and ERBB2 inhibitor).

For combination therapy, the nucleic acids of the invention can be prepared in at least one of two ways. First, the agents can be physically combined in a preparation of nucleic acid and chemotherapeutic agent, such as a mixture of a nucleic acid of the invention encapsulated in liposomes and ifosfamide in a solution for intravenous administration, wherein both agents are present in a therapeutically effective concentration (*e.g.*, ifosfamide in solution to deliver 1000-1250 mg/m²/day and liposome-associated nucleic acid of the invention in the same solution to deliver 0.1-100 mg/kg/day). Alternatively, the agents are administered separately but simultaneously in their respective effective doses (*e.g.*, 1000-1250 mg/m²/d ifosfamide and 0.1 to 100 mg/kg/day nucleic acid of the invention).

Those skilled in the art will recognize that other compounds and therapies used to treat the diseases and conditions described herein can similarly be combined with the nucleic acid molecules of the instant invention (*e.g.* siNA molecules) and are hence within the scope of the instant invention.

Example 11: Serum Stability for DsiRNAs

Serum stability of DsiRNA agents is assessed *via* incubation of DsiRNA agents in 50% fetal bovine serum for various periods of time (up to 24 h) at 37°C. Serum is extracted and the nucleic acids are separated on a 20% non-denaturing PAGE and can be visualized with Gelstar stain. Relative levels of protection from nuclease degradation are assessed for DsiRNAs (optionally with and without modifications).

Example 12: Use of Additional Cell Culture Models to Evaluate the Down-Regulation of EGFR Gene Expression

A variety of endpoints have been used in cell culture models to look at EGFR-mediated effects after treatment with anti-EGFR agents. Phenotypic endpoints include inhibition of cell proliferation, RNA expression, and reduction of EGFR protein expression.

Because EGFR mutations are directly associated with increased proliferation of certain tumor cells, a proliferation endpoint for cell culture assays is can be used as a screen. There are several methods by which this endpoint can be measured. Following treatment of cells with DsiRNA, cells are allowed to grow (typically 5 days), after which the cell viability, the incorporation of bromodeoxyuridine (BrdU) into cellular DNA and/or the cell density are measured. The assay of cell density can be done in a 96-well format using commercially available fluorescent nucleic acid stains (such as Syto[®] 13 or CyQuant[®]). As a secondary, confirmatory endpoint, a DsiRNA-mediated decrease in the level of EGFR protein expression can be evaluated using an EGFR-specific ELISA.

Example 13: Evaluation of Anti-EGFR DsiRNA Efficacy in a Mouse Model of EGFR Misregulation

Anti-EGFR DsiRNA chosen from *in vitro* assays can be further tested in mouse models, including, *e.g.*, xenograft and other animal models as recited above. In one example, mice possessing misregulated (*e.g.*, elevated) EGFR levels are administered a DsiRNA agent of the present invention *via* hydrodynamic tail vein injection. 3-4 mice per group (divided based upon specific DsiRNA agent tested) are injected with 50 µg or 200 µg of DsiRNA. Levels of EGFR RNA are evaluated using RT-qPCR. Additionally or alternatively, levels of EGFR (*e.g.*, EGFR protein levels or activity and/or cancer cell/tumor formation, growth or spread) can be evaluated using an art-recognized method, or phenotypes associated with misregulation of EGFR (*e.g.*, tumor formation, growth, metastasis, etc.) are monitored (optionally as a proxy for measurement of EGFR transcript or EGFR protein levels). Active DsiRNA in such animal models can also be subsequently tested in combination with standard chemotherapies.

Example 14: Diagnostic Uses

The DsiRNA molecules of the invention can be used in a variety of diagnostic applications, such as in the identification of molecular targets (*e.g.*, RNA) in a variety of applications, for example, in clinical, industrial, environmental, agricultural and/or research settings. Such diagnostic use of DsiRNA molecules involves utilizing reconstituted RNAi systems, for example, using cellular lysates or partially purified cellular lysates. DsiRNA molecules of this invention can be used as diagnostic tools to examine genetic drift and mutations within diseased cells. The close relationship between DsiRNA activity and the

structure of the target EGFR RNA allows the detection of mutations in a region of the EGFR molecule, which alters the base-pairing and three-dimensional structure of the target EGFR RNA. By using multiple DsiRNA molecules described in this invention, one can map nucleotide changes, which are important to RNA structure and function *in vitro*, as well as in cells and tissues. Cleavage of target EGFR RNAs with DsiRNA molecules can be used to inhibit gene expression and define the role of specified gene products in the progression of an EGFR-associated disease or disorder. In this manner, other genetic targets can be defined as important mediators of the disease. These experiments will lead to better treatment of the disease progression by affording the possibility of combination therapies (*e.g.*, multiple DsiRNA molecules targeted to different genes, DsiRNA molecules coupled with known small molecule inhibitors, or intermittent treatment with combinations of DsiRNA molecules and/or other chemical or biological molecules). Other *in vitro* uses of DsiRNA molecules of this invention are well known in the art, and include detection of the presence of RNAs associated with a disease or related condition. Such RNA is detected by determining the presence of a cleavage product after treatment with a DsiRNA using standard methodologies, for example, fluorescence resonance emission transfer (FRET).

In a specific example, DsiRNA molecules that cleave only wild-type or mutant or polymorphic forms of the target EGFR RNA are used for the assay. The first DsiRNA molecules (*i.e.*, those that cleave only wild-type forms of target EGFR RNA) are used to identify wild-type EGFR RNA present in the sample and the second DsiRNA molecules (*i.e.*, those that cleave only mutant or polymorphic forms of target RNA) are used to identify mutant or polymorphic EGFR RNA in the sample. As reaction controls, synthetic substrates of both wild-type and mutant or polymorphic EGFR RNA are cleaved by both DsiRNA molecules to demonstrate the relative DsiRNA efficiencies in the reactions and the absence of cleavage of the "non-targeted" EGFR RNA species. The cleavage products from the synthetic substrates also serve to generate size markers for the analysis of wild-type and mutant EGFR RNAs in the sample population. Thus, each analysis requires two DsiRNA molecules, two substrates and one unknown sample, which is combined into six reactions. The presence of cleavage products is determined using an RNase protection assay so that full-length and cleavage fragments of each EGFR RNA can be analyzed in one lane of a polyacrylamide gel. It is not absolutely required to quantify the results to gain insight into the expression of mutant or polymorphic EGFR RNAs and putative risk of EGFR-associated phenotypic changes in target cells. The expression of EGFR mRNA whose protein product is

implicated in the development of the phenotype (*i.e.*, disease related/associated) is adequate to establish risk. If probes of comparable specific activity are used for both transcripts, then a qualitative comparison of EGFR RNA levels is adequate and decreases the cost of the initial diagnosis. Higher mutant or polymorphic form to wild-type ratios are correlated with higher risk whether EGFR RNA levels are compared qualitatively or quantitatively.

All patents and publications mentioned in the specification are indicative of the levels of skill of those skilled in the art to which the invention pertains. All references cited in this disclosure are incorporated by reference to the same extent as if each reference had been incorporated by reference in its entirety individually.

One skilled in the art would readily appreciate that the present invention is well adapted to carry out the objects and obtain the ends and advantages mentioned, as well as those inherent therein. The methods and compositions described herein as presently representative of preferred embodiments are exemplary and are not intended as limitations on the scope of the invention. Changes therein and other uses will occur to those skilled in the art, which are encompassed within the spirit of the invention, are defined by the scope of the claims.

It will be readily apparent to one skilled in the art that varying substitutions and modifications can be made to the invention disclosed herein without departing from the scope and spirit of the invention. Thus, such additional embodiments are within the scope of the present invention and the following claims. The present invention teaches one skilled in the art to test various combinations and/or substitutions of chemical modifications described herein toward generating nucleic acid constructs with improved activity for mediating RNAi activity. Such improved activity can comprise improved stability, improved bioavailability, and/or improved activation of cellular responses mediating RNAi. Therefore, the specific embodiments described herein are not limiting and one skilled in the art can readily appreciate that specific combinations of the modifications described herein can be tested without undue experimentation toward identifying DsiRNA molecules with improved RNAi activity.

The invention illustratively described herein suitably can be practiced in the absence of any element or elements, limitation or limitations that are not specifically disclosed herein. Thus, for example, in each instance herein any of the terms "comprising", "consisting essentially of", and "consisting of" may be replaced with either of the other two terms. The

terms and expressions which have been employed are used as terms of description and not of limitation, and there is no intention that in the use of such terms and expressions of excluding any equivalents of the features shown and described or portions thereof, but it is recognized that various modifications are possible within the scope of the invention claimed. Thus, it should be understood that although the present invention has been specifically disclosed by preferred embodiments, optional features, modification and variation of the concepts herein disclosed may be resorted to by those skilled in the art, and that such modifications and variations are considered to be within the scope of this invention as defined by the description and the appended claims.

In addition, where features or aspects of the invention are described in terms of Markush groups or other grouping of alternatives, those skilled in the art will recognize that the invention is also thereby described in terms of any individual member or subgroup of members of the Markush group or other group.

The use of the terms "a" and "an" and "the" and similar referents in the context of describing the invention (especially in the context of the following claims) are to be construed to cover both the singular and the plural, unless otherwise indicated herein or clearly contradicted by context. The terms "comprising," "having," "including," and "containing" are to be construed as open-ended terms (i.e., meaning "including, but not limited to,") unless otherwise noted. Recitation of ranges of values herein are merely intended to serve as a shorthand method of referring individually to each separate value falling within the range, unless otherwise indicated herein, and each separate value is incorporated into the specification as if it were individually recited herein. All methods described herein can be performed in any suitable order unless otherwise indicated herein or otherwise clearly contradicted by context. The use of any and all examples, or exemplary language (e.g., "such as") provided herein, is intended merely to better illuminate the invention and does not pose a limitation on the scope of the invention unless otherwise claimed. No language in the specification should be construed as indicating any non-claimed element as essential to the practice of the invention.

Embodiments of this invention are described herein, including the best mode known to the inventors for carrying out the invention. Variations of those embodiments may become apparent to those of ordinary skill in the art upon reading the foregoing description.

The inventors expect skilled artisans to employ such variations as appropriate, and the inventors intend for the invention to be practiced otherwise than as specifically described

herein. Accordingly, this invention includes all modifications and equivalents of the subject matter recited in the claims appended hereto as permitted by applicable law. Moreover, any combination of the above-described elements in all possible variations thereof is encompassed by the invention unless otherwise indicated herein or otherwise clearly contradicted by context. Those skilled in the art will recognize, or be able to ascertain using no more than routine experimentation, many equivalents to the specific embodiments of the invention described herein. Such equivalents are intended to be encompassed by the following claims.

CLAIMS

We claim:

1. An isolated double stranded nucleic acid (dsNA) comprising ribonucleotides, consisting of: (a) a sense region and an antisense region, wherein said sense region and said antisense region together form a duplex region consisting of 25-35 base pairs and said antisense region comprises a sequence comprising at least 15 contiguous nucleotides that are complementary to a sequence selected from Table 17; and (b) from zero to two 3' overhang regions, wherein each overhang region is six or fewer nucleotides in length.
2. An isolated dsNA comprising ribonucleotides, consisting of: (a) a sense region and an antisense region, wherein said sense region and said antisense region together form a duplex region consisting of 25-35 base pairs and said antisense region comprises a sequence comprising at least 19 contiguous nucleotides that are complementary to a sequence selected from Tables 17 and 18; and (b) from zero to two 3' overhang regions, wherein each overhang region is six or fewer nucleotides in length.
3. An isolated dsNA comprising ribonucleotides, consisting of: (a) a sense region and an antisense region, wherein said sense region and said antisense region together form a duplex region consisting of 25-35 base pairs and said antisense region comprises a sequence that is the complement of a sequence selected from Tables 17-23; and (b) from zero to two 3' overhang regions, wherein each overhang region is six or fewer nucleotides in length.
4. An isolated dsNA comprising ribonucleotides, consisting of: (a) a sense region and an antisense region, wherein said sense region and said antisense region together form a duplex region consisting of 25-35 base pairs and said antisense region comprises a sequence that is the complement of a sequence selected from Tables 17-23; and (b) from zero to two 3' overhang regions, wherein each overhang region is six or fewer nucleotides in length, and wherein, starting from the 5' end (position 1) of a EGFR mRNA sequence selected from Tables 17-26 (position 1), mammalian Ago2 cleaves said mRNA at a site between positions 9 and 10 of said sequence.

5. An isolated dsNA comprising first and second nucleic acid strands comprising ribonucleotides and a duplex region of at least 25 base pairs, wherein said first strand is 25-34 nucleotides in length and comprises a 5'-terminus and a 3'-terminus and said second strand of said dsNA is 26-35 nucleotides in length and comprises a 5'-terminus and a 3'-terminus and comprises 1-5 single-stranded nucleotides at its 3' terminus, wherein said second oligonucleotide strand is sufficiently complementary to a target EGFR mRNA sequence selected from the group consisting of Tables 17-26 and SEQ ID NOs: 2137-2396 along at least 19 nucleotides of said second oligonucleotide strand length to reduce EGFR target gene expression when said double stranded nucleic acid is introduced into a mammalian cell.
6. An isolated dsNA comprising first and second nucleic acid strands comprising ribonucleotides and a duplex region of at least 25 base pairs, wherein said first strand is 25-34 nucleotides in length and said second strand of said dsNA is 26-35 nucleotides in length and comprises 1-5 single-stranded nucleotides at its 3' terminus, wherein the 3' terminus of said first oligonucleotide strand and the 5' terminus of said second oligonucleotide strand form a blunt end, and said second oligonucleotide strand is sufficiently complementary to a target EGFR sequence selected from the group consisting of Tables 17-26 and SEQ ID NOs: 2137-2396 along at least 19 nucleotides of said second oligonucleotide strand length to reduce EGFR mRNA expression when said double stranded nucleic acid is introduced into a mammalian cell.
7. The isolated dsNA of any of claims 1-4, comprising a first oligonucleotide strand comprising a 5'-terminus and a 3'-terminus and said second oligonucleotide strand comprising a 5'-terminus and a 3'-terminus.
8. The isolated dsNA of claim 7, wherein said second oligonucleotide strand comprises 1-5 single-stranded nucleotides at its 3' terminus.
9. The isolated dsNA of any of claims 5, 6 and 8, wherein said 3' overhang is 1-3 nucleotides in length.
10. The isolated dsNA of any of claims 5, 6 and 8, wherein said nucleotides of said 3' overhang comprise a modified nucleotide.

11. The isolated dsNA of claim 10, wherein said modified nucleotide of said 3' overhang is a 2'-O-methyl ribonucleotide.
12. The isolated dsNA of claim 10 wherein said modified nucleotide residues are selected from the group consisting of 2'-O-methyl, 2'-methoxyethoxy, 2'-fluoro, 2'-allyl, 2'-O-[2-(methylamino)-2-oxoethyl], 4'-thio, 4'-CH₂-O-2'-bridge, 4'-(CH₂)₂-O-2'-bridge, 2'-LNA, 2'-amino and 2'-O-(N-methylcarbamate).
13. The isolated dsNA of claim 10, wherein said 3' overhang is two nucleotides in length and wherein said modified nucleotide of said 3' overhang is a 2'-O-methyl modified ribonucleotide.
14. The isolated dsNA of any of claims 5, 6 and 8, wherein all nucleotides of said 3' overhang are modified nucleotides.
15. The isolated dsNA of any of the preceding claims, wherein said dsNA reduces EGFR mRNA levels by at least 80% when assayed *in vitro* in a mammalian cell at an effective concentration in the environment of said cell of 1 nanomolar or less.
16. The isolated dsNA of any of claims 5-15, wherein said second oligonucleotide strand is complementary to target EGFR cDNA sequence NM_005228.3 along at most 27 nucleotides of said second oligonucleotide strand length.
17. The isolated dsNA of any of claims 5-16, wherein said second strand comprises a sequence selected from the group consisting of SEQ ID NOs: 357-616.
18. The isolated dsNA of any of claims 5-17, wherein said first strand comprises a sequence selected from the group consisting of SEQ ID NOs: 1-260, 1069-1328, 1781-2040 and 2137-2396.

19. The isolated dsNA of any of claims 5-18 comprising a pair of first strand/second strand sequences selected from the group consisting of DsiRNA agents shown in Table 2, 3, 7 and 9.
20. The isolated dsNA of any of claims 5-19, wherein starting from the first nucleotide (position 1) at the 3' terminus of the first oligonucleotide strand, position 1, 2 and/or 3 is substituted with a modified nucleotide.
21. The isolated dsNA of claim 20, wherein said modified nucleotide residue of said 3' terminus of said first strand is selected from the group consisting of a deoxyribonucleotide, an acyclonucleotide and a fluorescent molecule.
22. The isolated dsNA of claim 20, wherein position 1 of said 3' terminus of the first oligonucleotide strand is a deoxyribonucleotide.
23. The isolated dsNA of any of claims 5 and 7-22, wherein said 3' terminus of said first strand and said 5' terminus of said second strand form a blunt end.
24. The isolated dsNA of any of claims 5-23, wherein said first strand is 25 nucleotides in length and said second strand is 27 nucleotides in length.
25. The isolated dsNA of any of claims 7-23, wherein said second strand has a length which is at least 26 nucleotides.
26. The isolated dsNA of any of claims 1-3 and 5-25, wherein, starting from the 5' end of a EGFR mRNA sequence selected from Table 16 (position 1), mammalian Ago2 cleaves said mRNA at a site between positions 9 and 10 of said sequence, thereby reducing EGFR target mRNA expression when said double stranded nucleic acid is introduced into a mammalian cell.
27. The isolated dsNA of any of the preceding claims, wherein, starting from the 5' end of a EGFR mRNA sequence selected from Table 6, mammalian Ago2 cleaves said mRNA at a site between positions 9 and 10 of said mRNA sequence, thereby reducing EGFR target

mRNA expression when said double stranded nucleic acid is introduced into a mammalian cell.

28. The isolated dsNA of any of claims 5-27, wherein each of said first and said second strands has a length which is at least 26 nucleotides.

29. The isolated dsNA of any of the preceding claims, wherein said dsNA comprises a modified nucleotide.

30. The isolated dsNA of claim 29, wherein said modified nucleotide residue is selected from the group consisting of 2'-O-methyl, 2'-methoxyethoxy, 2'-fluoro, 2'-allyl, 2'-O-[2-(methylamino)-2-oxoethyl], 4'-thio, 4'-CH₂-O-2'-bridge, 4'-(CH₂)₂-O-2'-bridge, 2'-LNA, 2'-amino and 2'-O-(N-methylcarbamate).

31. The isolated dsNA of any of claims 5-30, wherein said second oligonucleotide strand, starting from the nucleotide residue of said second strand that is complementary to the 5' terminal nucleotide residue of said first oligonucleotide strand, comprises alternating modified and unmodified nucleotide residues.

32. The isolated dsNA of any of claims 5-31, wherein said second oligonucleotide strand, starting from the nucleotide residue of said second strand that is complementary to the 5' terminal nucleotide residue of said first oligonucleotide strand, comprises unmodified nucleotide residues at all positions from position 18 to the 5' terminus of said second oligonucleotide strand.

33. The isolated dsNA of any of claims 5-32, wherein said second oligonucleotide strand comprises a modification pattern selected from the group consisting of AS-M1 to AS-M41 and AS-M1* to AS-M41*.

34. The isolated dsNA of any of claims 5-33, wherein said first oligonucleotide strand comprises a modification pattern selected from the group consisting of SM1 to SM16.

35. The isolated dsNA of any of claims 5-34, wherein each of said first and said second strands has a length which is at least 26 and at most 30 nucleotides.
36. The isolated dsNA of any of the preceding claims, wherein said dsNA is cleaved endogenously in said cell by Dicer.
37. The isolated dsNA of any of the preceding claims, wherein the amount of said isolated nucleic acid sufficient to reduce expression of the target gene is selected from the group consisting of 1 nanomolar or less, 200 picomolar or less, 100 picomolar or less, 50 picomolar or less, 20 picomolar or less, 10 picomolar or less, 5 picomolar or less, 2, picomolar or less and 1 picomolar or less in the environment of said cell.
38. The isolated dsNA of any of claims 2-37, wherein said isolated dsNA possesses greater potency than an isolated 21mer siRNA directed to the identical at least 19 nucleotides of said target EGFR mRNA in reducing target EGFR mRNA expression when assayed *in vitro* in a mammalian cell at an effective concentration in the environment of a cell selected from the group consisting of 1 nanomolar or less, 300 picomolar or less, 200 picomolar or less, 100 picomolar or less, 50 picomolar or less, 20 picomolar or less, 10 picomolar or less, 5 picomolar or less, 2, picomolar or less and 1 picomolar or less in the environment of said cell.
39. The isolated dsNA of any of the above claims, wherein said isolated dsNA is sufficiently complementary to the target EGFR mRNA sequence to reduce EGFR target mRNA expression by an amount (expressed by %) selected from the group consisting of at least 10%, at least 50%, at least 80-90%, at least 95%, at least 98%, and at least 99% when said double stranded nucleic acid is introduced into a mammalian cell.
40. The isolated dsNA of any of claims 5-39, wherein the first and second strands are joined by a chemical linker.
41. The isolated double stranded nucleic acid of any of claims 5-40, wherein said 3' terminus of said first strand and said 5' terminus of said second strand are joined by a chemical linker.

42. The isolated double stranded nucleic acid of any of claims 5-41, wherein a nucleotide of said second or first strand is substituted with a modified nucleotide that directs the orientation of Dicer cleavage.

43. The isolated nucleic acid of any of the preceding claims comprising a modified nucleotide selected from the group consisting of a deoxyribonucleotide, a dideoxyribonucleotide, an acyclonucleotide, a 3'-deoxyadenosine (cordycepin), a 3'-azido-3'-deoxythymidine (AZT), a 2',3'-dideoxyinosine (ddI), a 2',3'-dideoxy-3'-thiacytidine (3TC), a 2',3'-didehydro-2',3'-dideoxythymidine (d4T), a monophosphate nucleotide of 3'-azido-3'-deoxythymidine (AZT), a 2',3'-dideoxy-3'-thiacytidine (3TC) and a monophosphate nucleotide of 2',3'-didehydro-2',3'-dideoxythymidine (d4T), a 4-thiouracil, a 5-bromouracil, a 5-iodouracil, a 5-(3-aminoallyl)-uracil, a 2'-O-alkyl ribonucleotide, a 2'-O-methyl ribonucleotide, a 2'-amino ribonucleotide, a 2'-fluoro ribonucleotide, and a locked nucleic acid.

44. The isolated nucleic acid of any of the preceding claims comprising a phosphate backbone modification selected from the group consisting of a phosphonate, a phosphorothioate and a phosphotriester.

45. The isolated nucleic acid of any of the preceding claims comprising a modification selected from the group consisting of a morpholino nucleic acid and a peptide nucleic acid (PNA).

46. The isolated double stranded nucleic acid of any of the above claims, wherein said second oligonucleotide strand is sufficiently complementary to a target EGFR cDNA sequence selected from the group consisting of the sequences shown in Table 13 along at least 19 nucleotides of said second oligonucleotide strand length to reduce EGFR target gene expression when said double stranded nucleic acid is introduced into a mammalian cell.

47. An isolated double stranded ribonucleic acid (dsNA) comprising first and second nucleic acid strands, wherein said dsNA comprises a blunt end, wherein each of said first and second oligonucleotide strands consists of the same number of nucleotide residues and is at most 35 nucleotides in length, wherein the ultimate and penultimate residues of said 3'

terminus of said first strand and the ultimate and penultimate residues of said 5' terminus of said second strand form one or two mismatched based pairs, wherein said second oligonucleotide strand is sufficiently complementary to a target EGFR cDNA sequence selected from Table 13 along at least 15 nucleotides of said second oligonucleotide strand length to reduce EGFR target gene expression when said double stranded nucleic acid is introduced into a mammalian cell, wherein said dsNA reduces EGFR mRNA levels by at least 70% when assayed *in vitro* in a mammalian cell at an effective concentration in the environment of said cell of 1 nanomolar or less.

48. An isolated dsNA of claim 47 comprising a duplex region of at least 25 base pairs.

49. The isolated dsNA of claim 47, wherein each of said first strand and said second strand is 25-35 nucleotides in length.

50. The isolated dsNA of claim 49, wherein said first strand comprises a sequence selected from the group consisting of SEQ ID NOs: 1-260, 1069-1328, 1781-2040 and 2137-2396.

51. A method for reducing expression of a target EGFR gene in a mammalian cell comprising contacting a mammalian cell *in vitro* with an isolated dsNA of any of the preceding claims in an amount sufficient to reduce expression of a target EGFR gene in said cell.

52. The method of claim 51, wherein target EGFR gene expression is reduced by an amount (expressed by %) selected from the group consisting of at least 10%, at least 50% and at least 80-90%.

53. The method of claim 51, wherein EGFR mRNA levels are reduced by an amount (expressed by %) of at least 90% at least 8 days after said cell is contacted with said dsNA.

54. The method of claim 51, wherein EGFR mRNA levels are reduced by an amount (expressed by %) of at least 70% at least 10 days after said cell is contacted with said dsNA.

55. A method for reducing expression of a target EGFR gene in a mammal comprising administering an isolated dsNA of any of claims 1-50 to a mammal in an amount sufficient to reduce expression of a target EGFR gene in the mammal.

56. The method of claim 55, wherein said isolated dsNA is administered at a dosage selected from the group consisting of 1 microgram to 5 milligrams per kilogram of said mammal per day, 100 micrograms to 0.5 milligrams per kilogram, 0.001 to 0.25 milligrams per kilogram, 0.01 to 20 micrograms per kilogram, 0.01 to 10 micrograms per kilogram, 0.10 to 5 micrograms per kilogram, and 0.1 to 2.5 micrograms per kilogram.

57. The method of claim 55, wherein said isolated dsNA possesses greater potency than an isolated 21mer siRNA directed to the identical at least 15 nucleotides of said target EGFR mRNA in reducing target EGFR gene expression when assayed *in vitro* in a mammalian cell at an effective concentration in the environment of a cell of 1 nanomolar or less.

58. The method of claim 55, wherein said administering step comprises a mode selected from the group consisting of intravenous injection, intramuscular injection, intraperitoneal injection, infusion, subcutaneous injection, transdermal, aerosol, rectal, vaginal, topical, oral and inhaled delivery.

59. A method for selectively inhibiting the growth of a cell comprising contacting a cell with an amount of an isolated dsNA of any of claims 1-50 sufficient to inhibit the growth of the cell.

60. The method of claim 59, wherein said cell is a tumor cell of a subject.

61. The method of claim 59, wherein said cell is a non-small cell lung cancer cell.

62. The method of claim 61, wherein said non-small cell lung cancer cell is erlotinib resistant.

63. The method of claim 61, wherein said non-small cell lung cancer cell does not comprise a KRAS mutation.

64. The method of claim 59, wherein the growth of said cell is inhibited by an amount selected from the group consisting of at least 15%, at least 25%, at least 40% and at least 50%, as compared to an appropriate control.

65. The method of claim 59, wherein said cell is a tumor cell *in vitro*.

66. The method of claim 59, wherein said cell is a human cell.

67. A method for treating or preventing an EGFR-associated disease or disorder in a subject comprising administering the isolated dsNA of any of claims 1-50 and a pharmaceutically acceptable carrier to the subject in an amount sufficient to treat or prevent said EGFR-associated disease or disorder in said subject, thereby treating or preventing said EGFR-associated disease or disorder in said subject.

68. The method of claim 67, wherein said EGFR-associated disease or disorder is selected from the group consisting of squamous cell carcinoma of the head and neck (SCCHN), lung and colorectal cancer.

69. A formulation comprising the isolated dsNA of any of claims 1-50, wherein said dsNA is present in an amount effective to reduce target EGFR RNA levels when said dsNA is introduced into a mammalian cell *in vitro* by an amount (expressed by %) selected from the group consisting of at least 10%, at least 50% and at least 80-90%, and wherein said dsNA possesses greater potency than an isolated 21mer siRNA directed to the identical at least 15 nucleotides of said target EGFR cDNA in reducing target EGFR RNA levels when assayed *in vitro* in a mammalian cell at an effective concentration in the environment of a cell of 1 nanomolar or less.

70. The formulation of claim 69, wherein said effective amount is selected from the group consisting of 1 nanomolar or less, 200 picomolar or less, 100 picomolar or less, 50 picomolar or less, 20 picomolar or less, 10 picomolar or less, 5 picomolar or less, 2, picomolar or less and 1 picomolar or less in the environment of said cell.

71. A formulation comprising the isolated dsNA of any of claims 1-50, wherein said dsNA is present in an amount effective to reduce target EGFR RNA levels when said dsNA is introduced into a cell of a mammalian subject by an amount (expressed by %) selected from the group consisting of at least 10%, at least 50% and at least 80-90%, and wherein said dsNA possesses greater potency than an isolated 21mer siRNA directed to the identical at least 15 nucleotides of said target EGFR cDNA in reducing target EGFR RNA levels when assayed *in vitro* in a mammalian cell at an effective concentration in the environment of a cell of 1 nanomolar or less.
72. The formulation of claim 71, wherein said effective amount is a dosage selected from the group consisting of 1 microgram to 5 milligrams per kilogram of said subject per day, 100 micrograms to 0.5 milligrams per kilogram, 0.001 to 0.25 milligrams per kilogram, 0.01 to 20 micrograms per kilogram, 0.01 to 10 micrograms per kilogram, 0.10 to 5 micrograms per kilogram, and 0.1 to 2.5 micrograms per kilogram.
73. A mammalian cell containing the isolated dsNA of any of claims 1-50.
74. A pharmaceutical composition comprising the isolated dsNA of any of claims 1-50 and a pharmaceutically acceptable carrier.
75. A kit comprising the isolated dsNA of any of claims 1-50 and instructions for its use.
76. A composition possessing EGFR inhibitory activity consisting essentially of an isolated dsNA of any of claims 1-50.

Figure 1

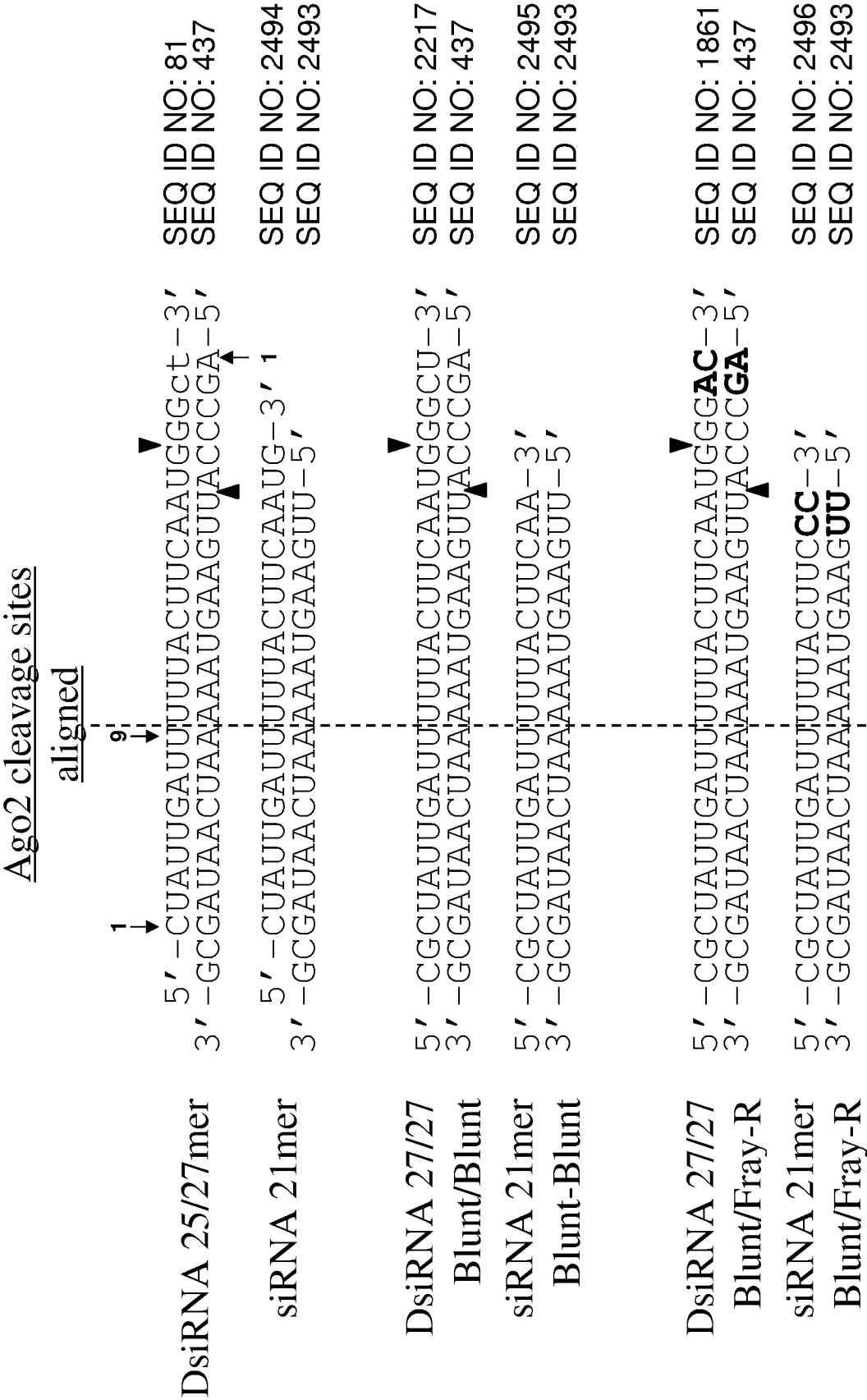


Figure 2A
DsiRNA-mediated Knockdown of EGFR in HeLa Cells, Primary Screen
Human EGFR-specific DsiRNAs
Normalized to HPRT and SFRS9; vs NC1, NC5, NC

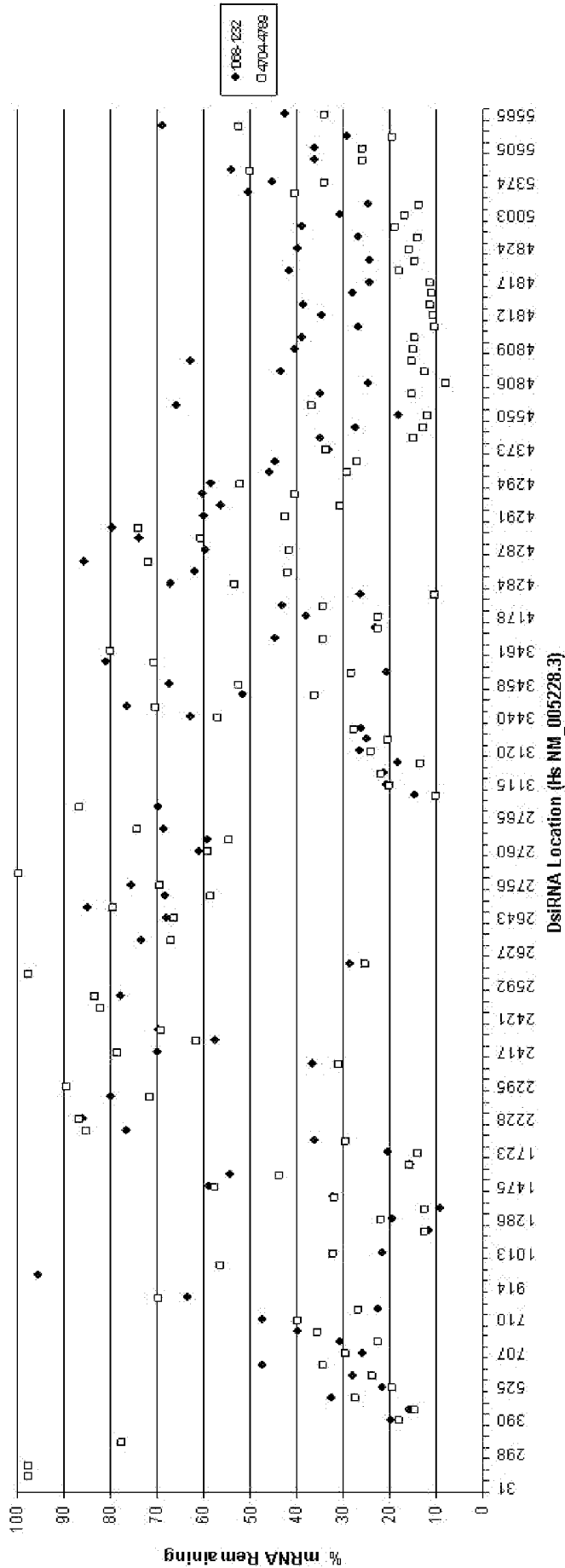


Figure 2B
DsiRNA-mediated Knockdown of EGFR in HeLa Cells, Primary Screen
Human and Mouse EGFR-targeting DsiRNAs
Normalized to HPRT and SFRS9; vs NC1, NC5, NC

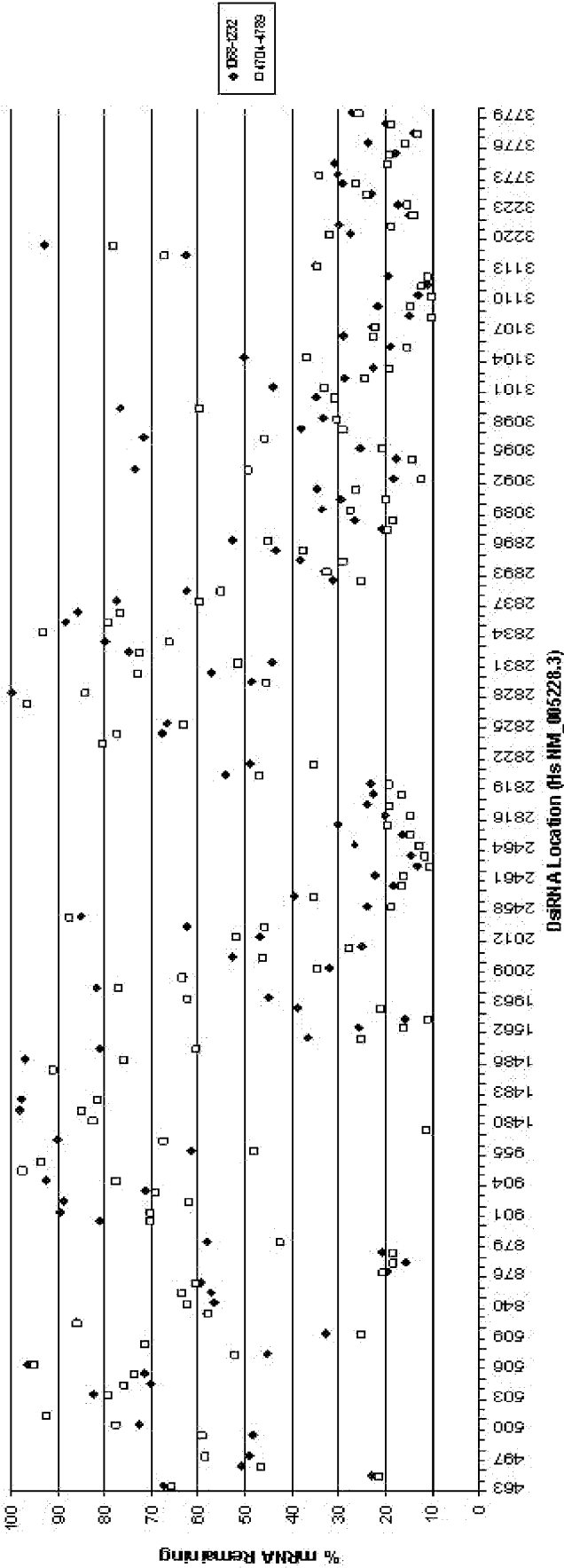


Figure 2C

DsiRNA-mediated Knockdown of EGFR in Mouse Hepa1-6 Cells, Primary Screen
Mouse EGFR-specific DsiRNAs
Normalized to HPRT and Rpl23; vs NC1, NC5, NC

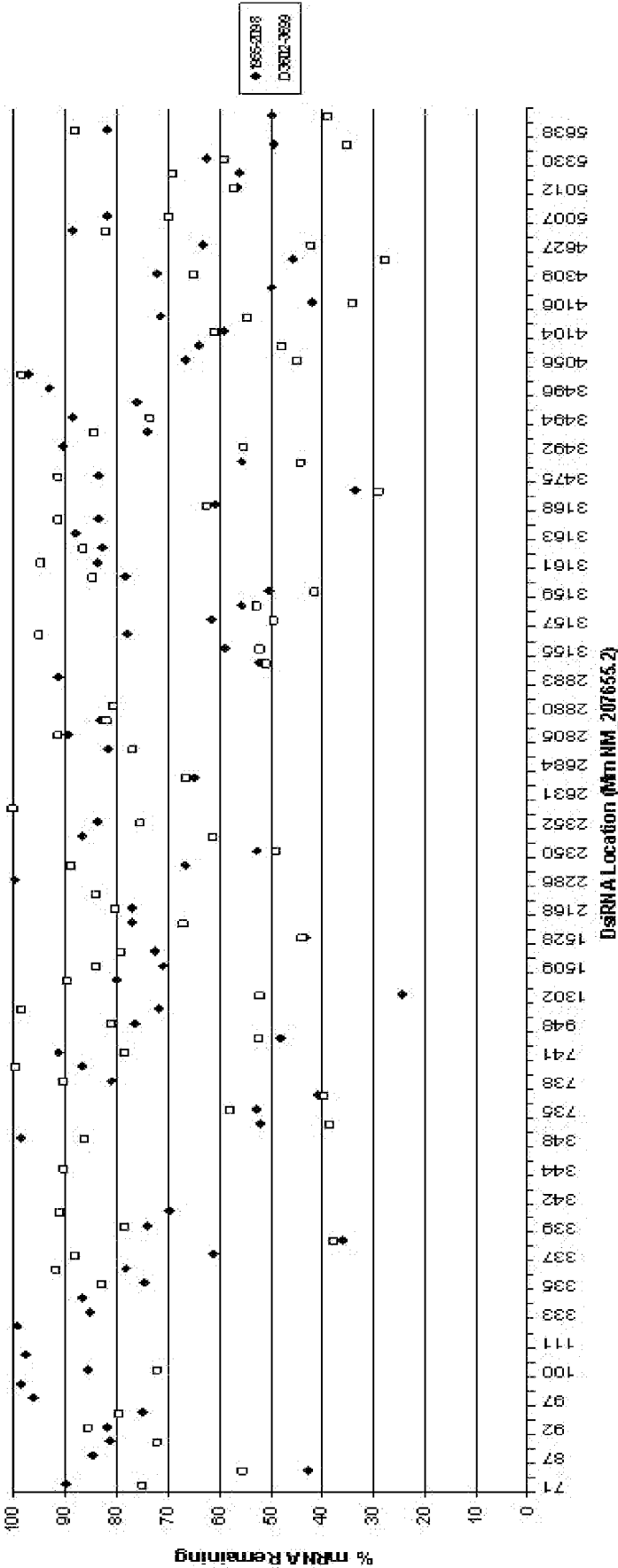


Figure 2D
DsiRNA-mediated Knockdown of EGFR in Mouse Hepa1-6 Cells, Primary Screen
Human and Mouse EGFR-targeting DsiRNAs
Normalized to HPRT and Rpl23; vs NC1, NC5, NC

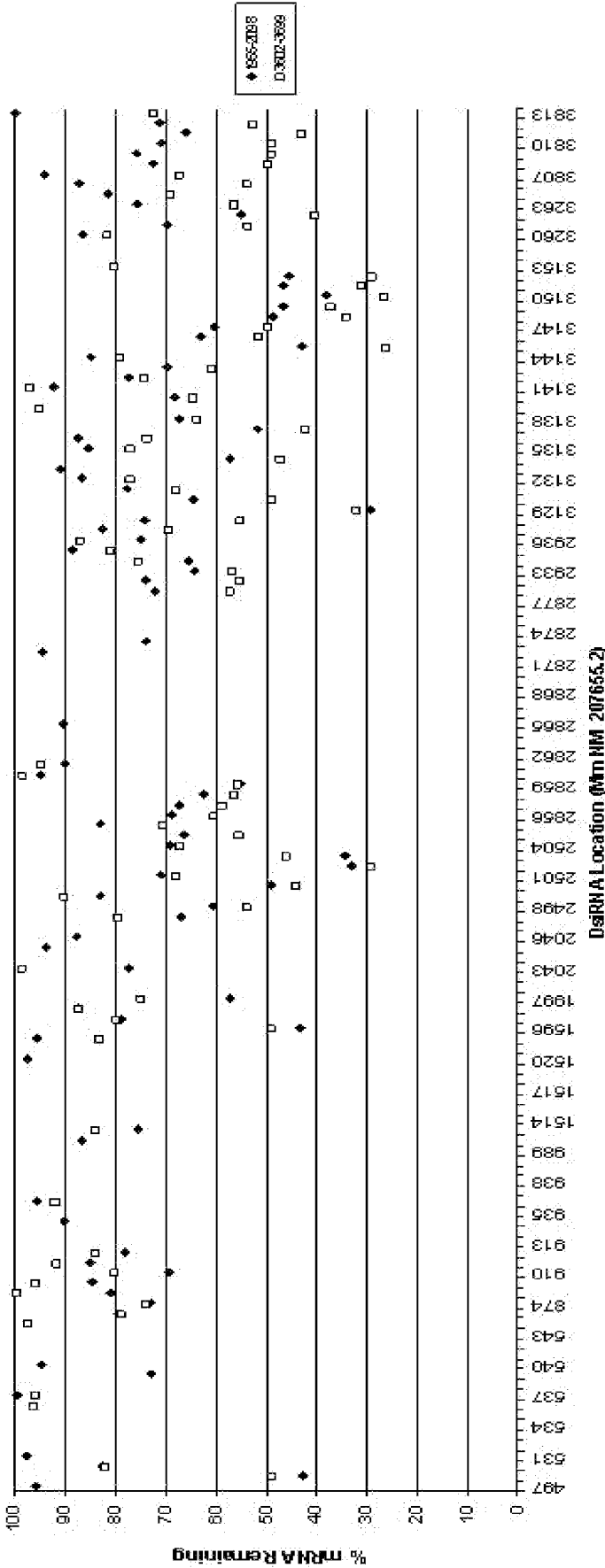
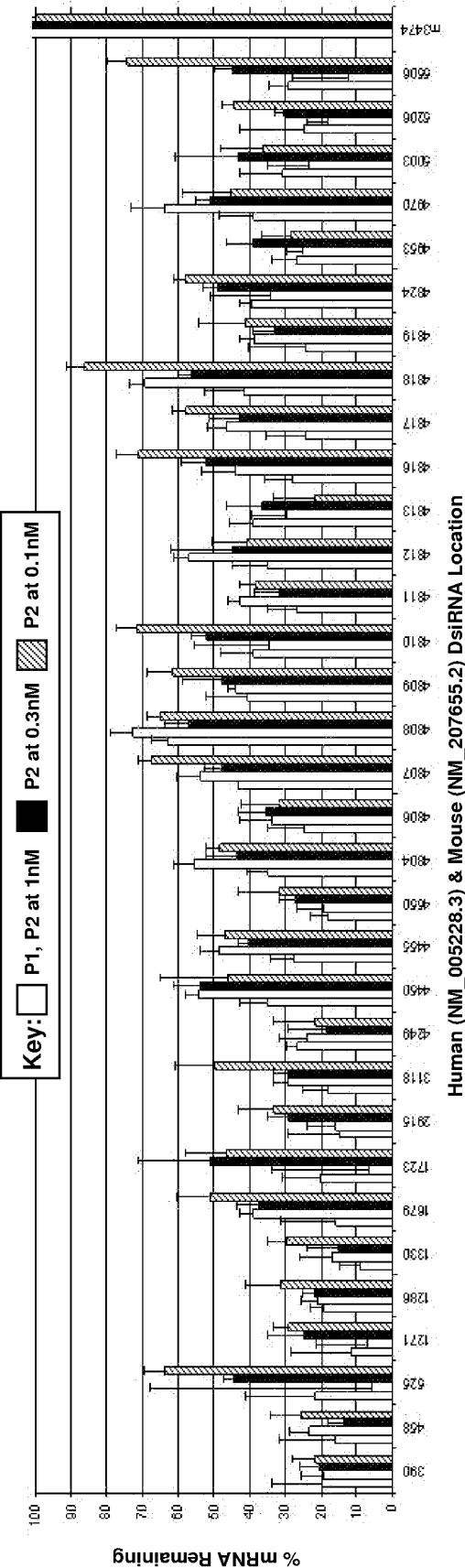


Figure 3A

Human and Mouse EGFR Knockdown - Human (HeLa) Cells - Phase 2
Normalized to HPRT and SFRS9; vs NC1, NC5, NC7

Assay: Hs EGFR 1068-1232 (FAM)



Assay: Hs EGFR 4704-4789 (Yakima Yellow)

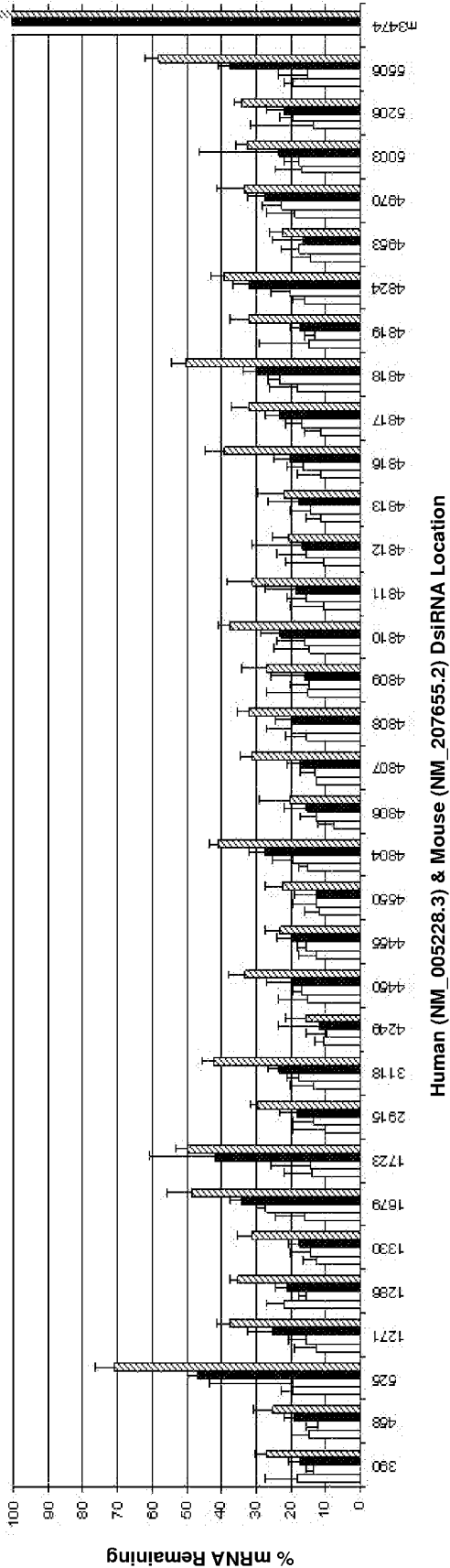


Figure 3B

Human EGFR Knockdown - Human (HeLa) Cells - Phase 2
Normalized to HPRT and SFRS9; vs NC1, NC5, NC7

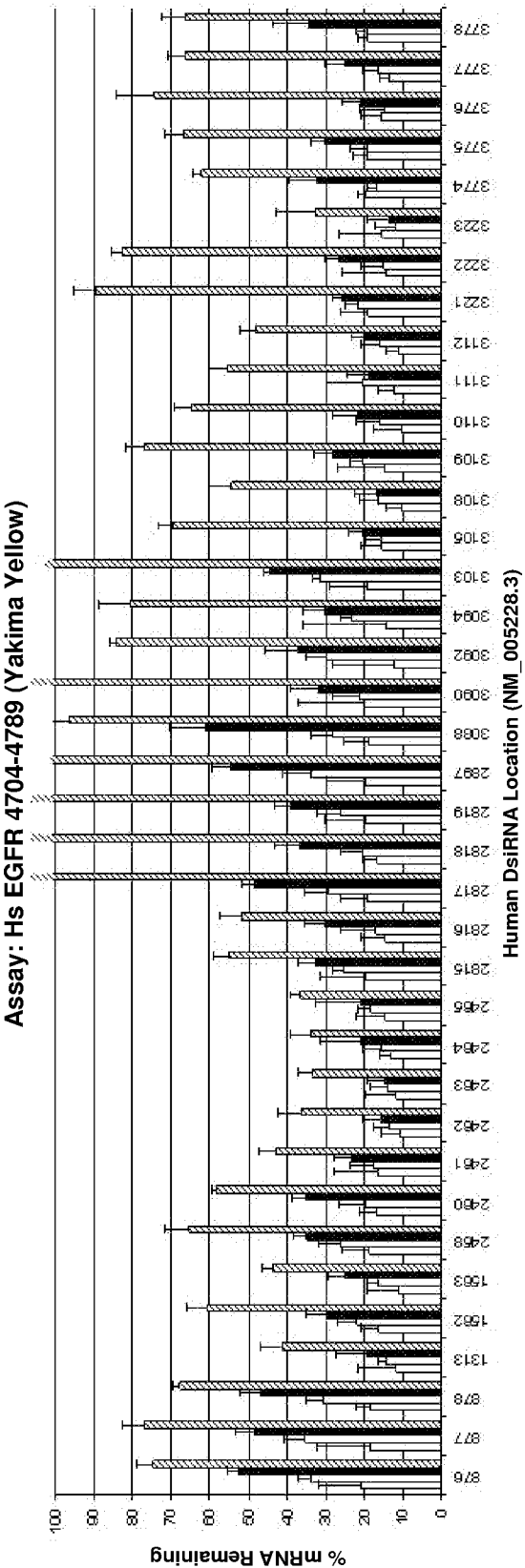
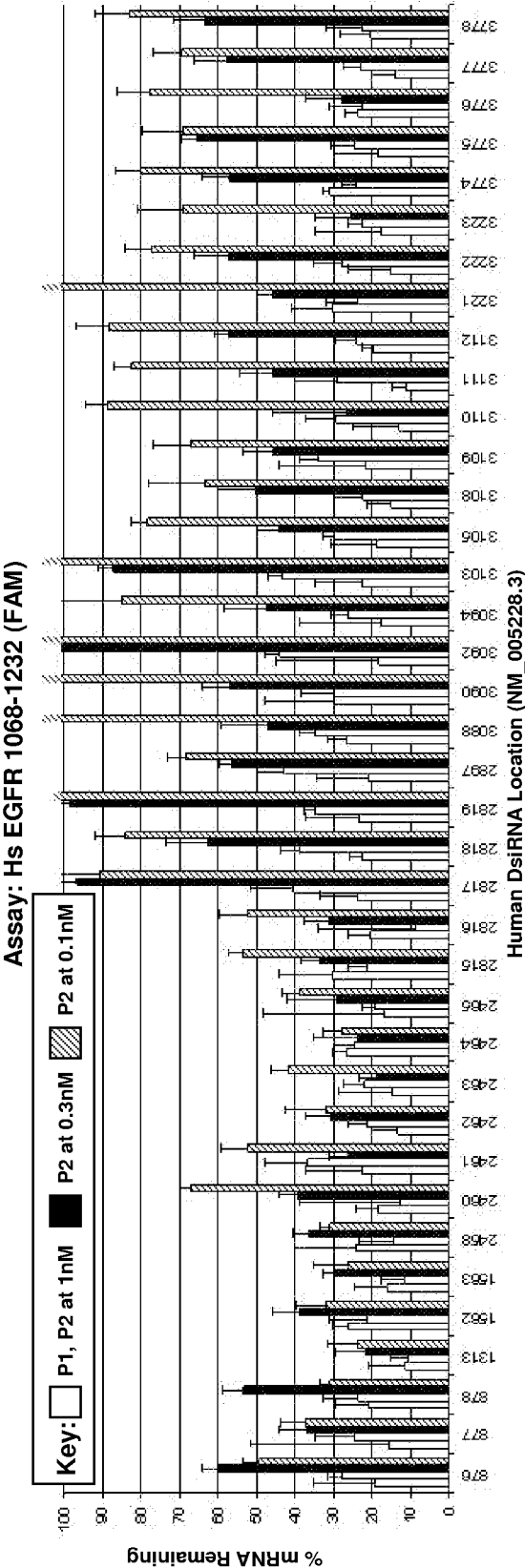
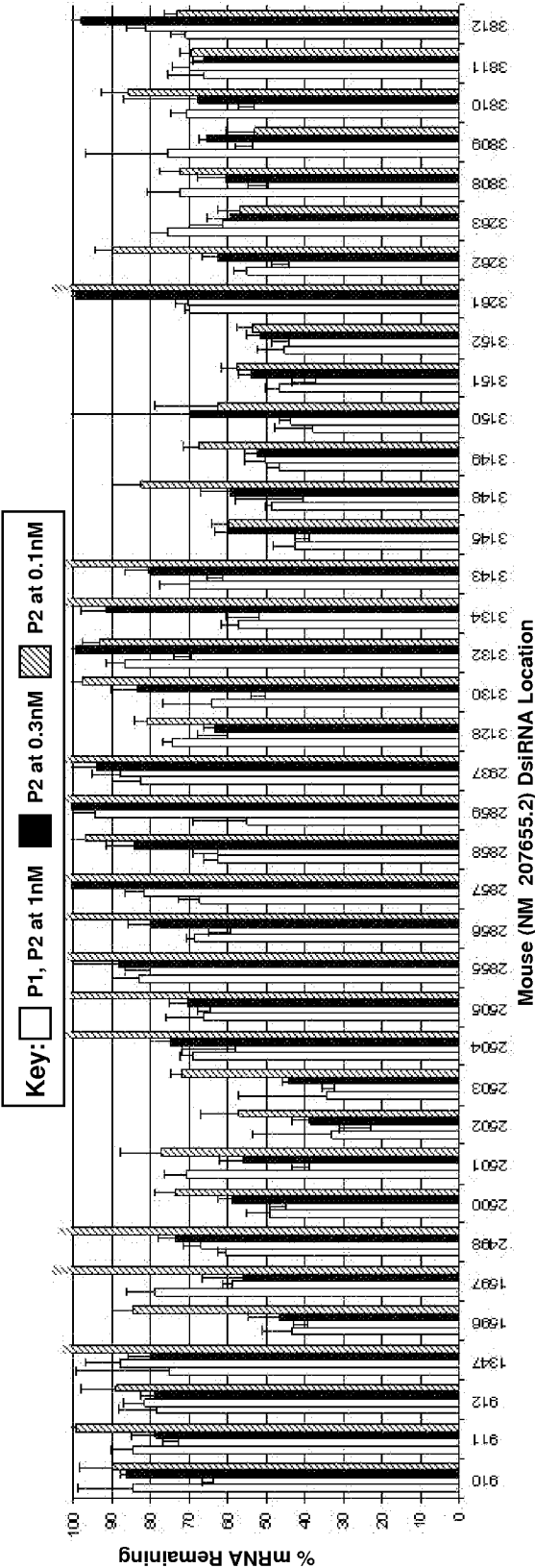


Figure 3C

Mouse EGFR Knockdown - Mouse (Hepa1-6) Cells - Phase 2
Normalized to HPRT and Rpl23; vs NC1, NC5, NC7
Assay: Mm EGFR 1955-2098 (Yakima Yellow)



Assay: Mm EGFR 3602-3699 (FAM)

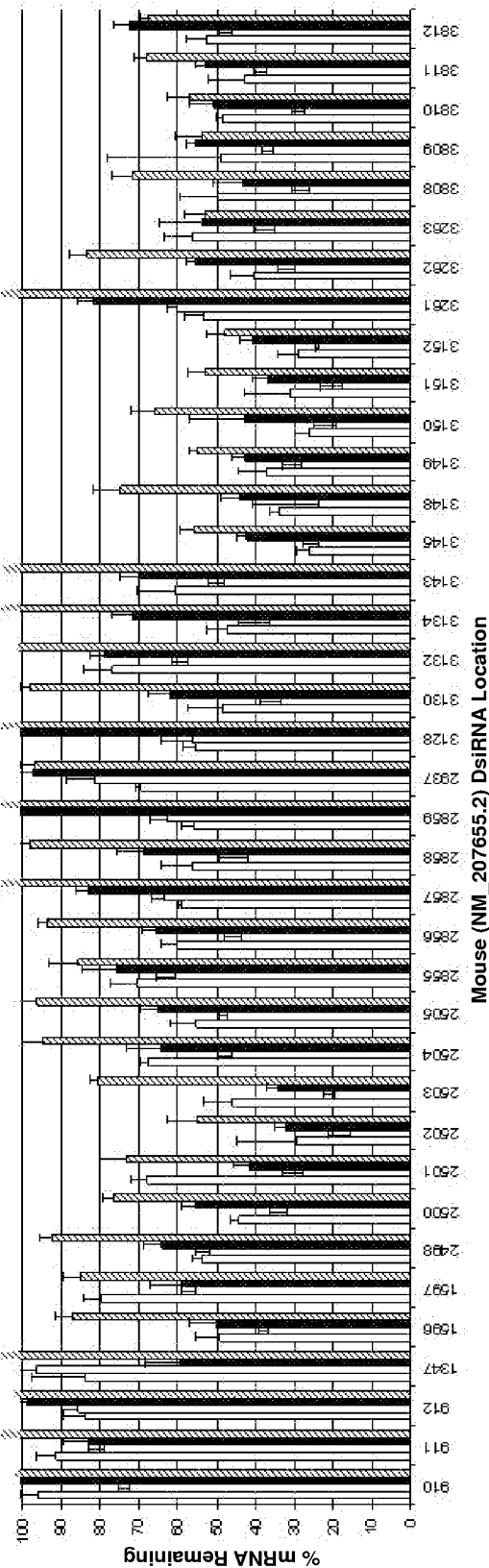


Figure 3D
Mouse EGFR Knockdown - Mouse (Hepa1-6) Cells - Phase 2
Normalized to HPRT and Rpl23; vs NC1, NC5, NC7
Assay: Mm EGFR 1955-2098 (Yakima Yellow)

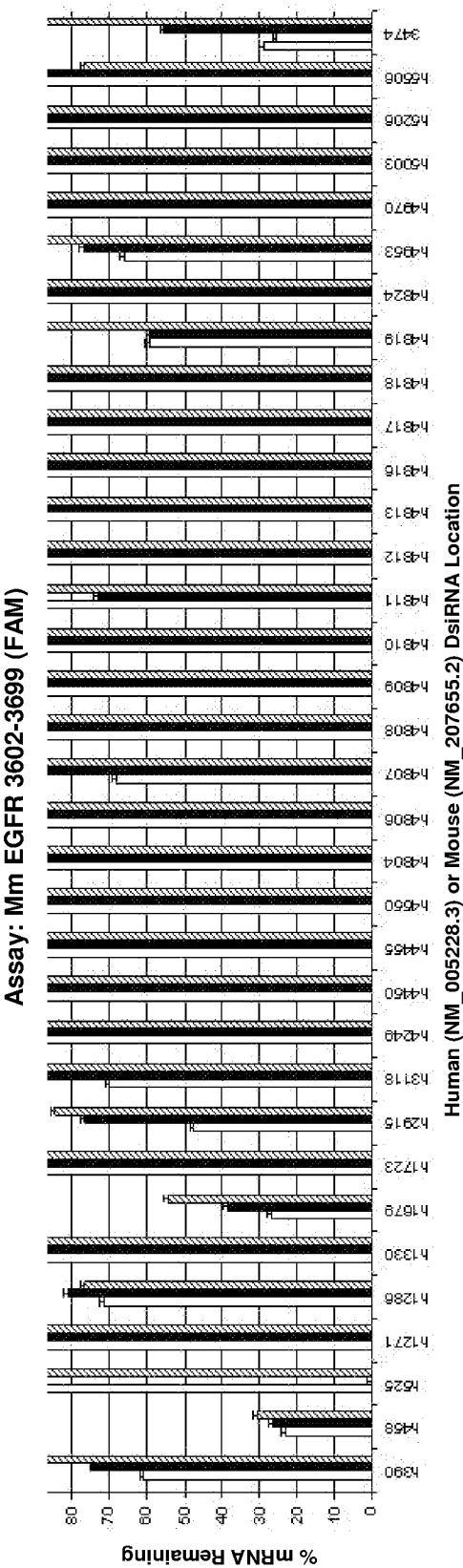
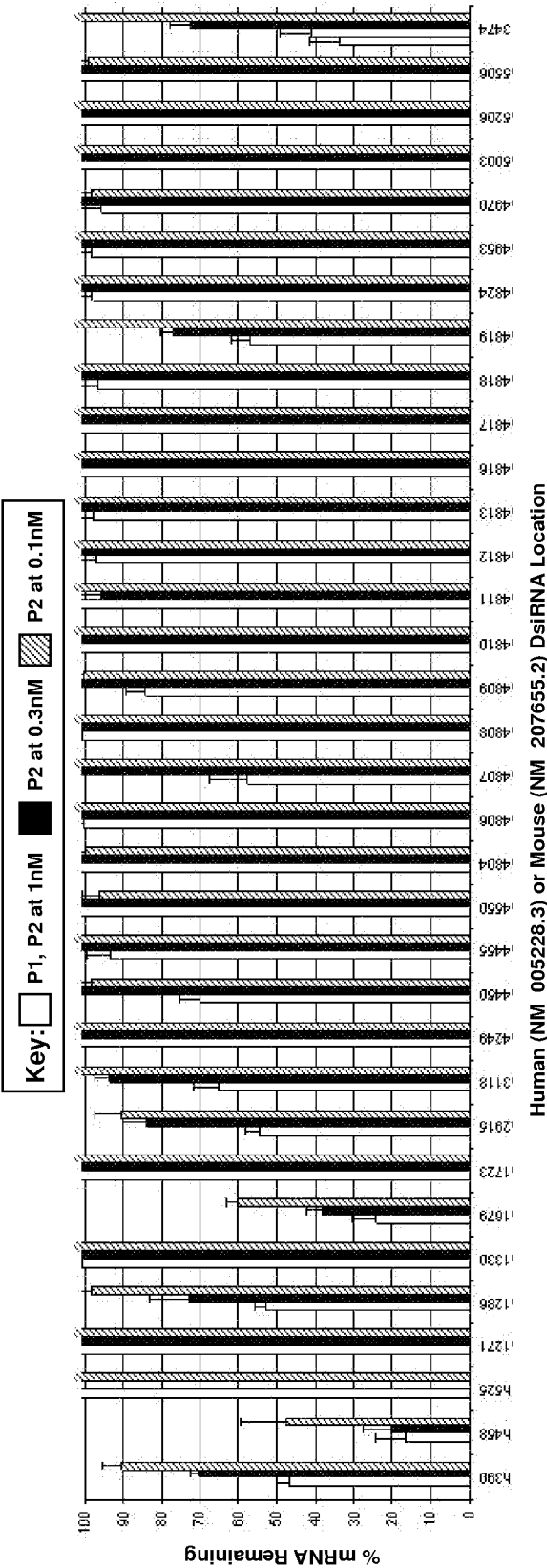


Figure 4A
Antisense (Guide) Strand 2'-OMe Modification Patterns

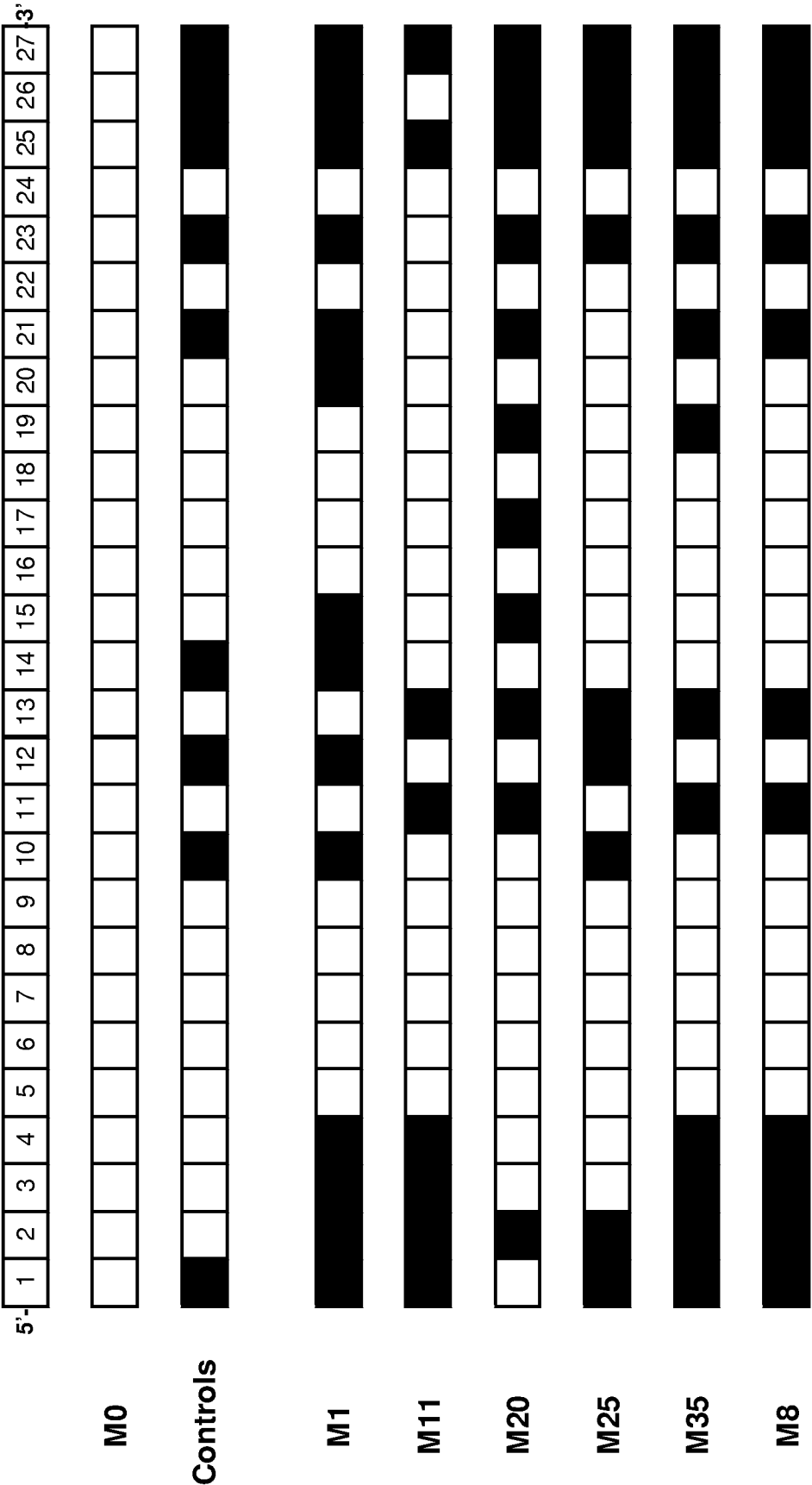


Figure 4B

Human EGFR Knockdown in Human HeLa Cells – Phase 3
Normalized to Hs HPRT 517-591 (FAM) and Hs SFRS9 569-712 (MAX) vs M8INC1, M8INC5, M8INC7
DsiRNAs: EGFR-878, EGFR-1313, EGFR-1563, EGFR-2458

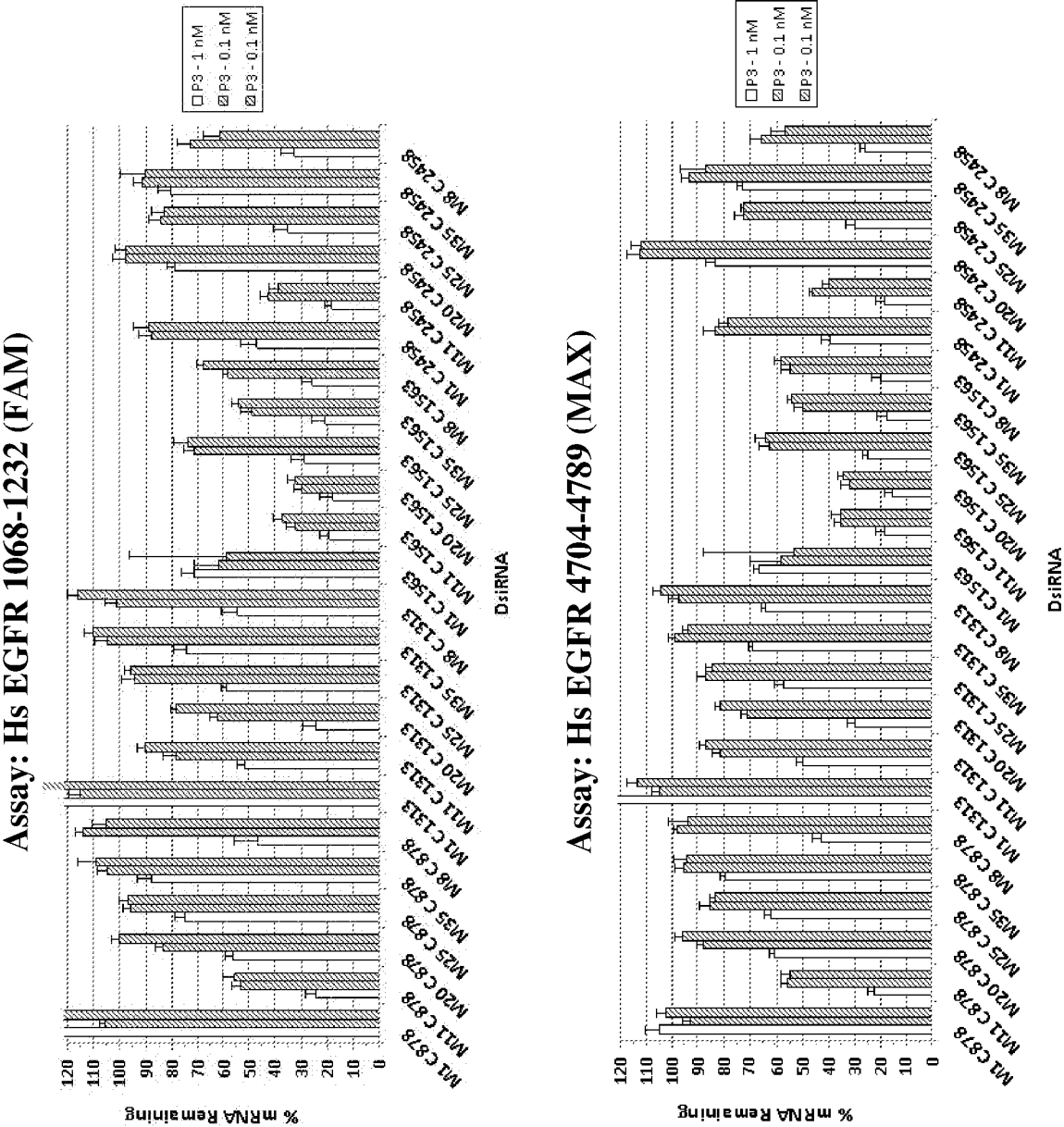
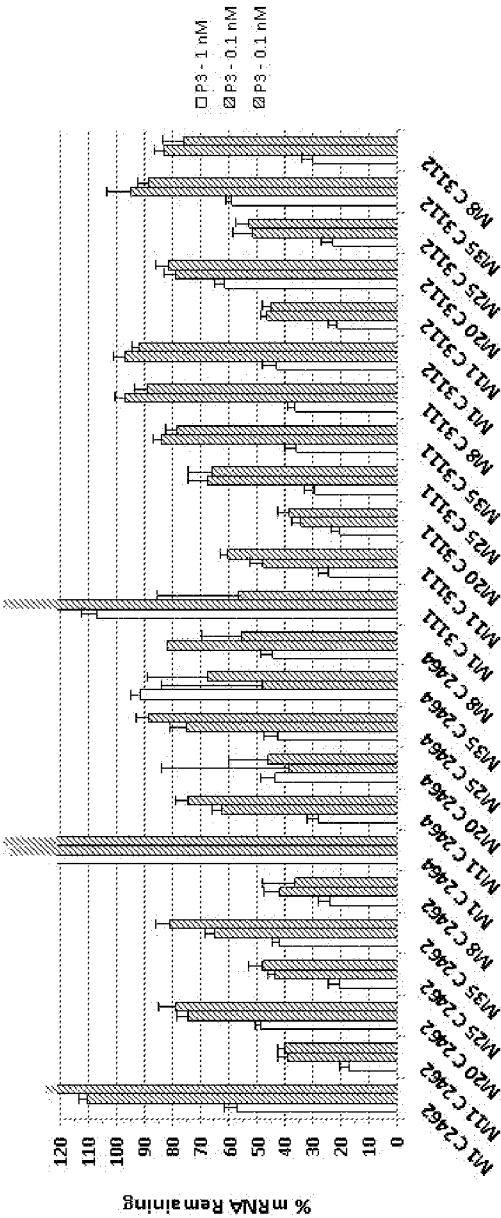


Figure 4C
Human EGFR Knockdown in Human HeLa Cells – Phase 3
Normalized to Hs HPRT 517-591 (FAM) and Hs SFRS9 569-712 (MAX) vs M8INC1, M8INC5, M8INC7
DsiRNAs: EGFR-2462, EGFR-2464, EGFR-3111, EGFR-3112
Assay: Hs EGFR 1068-1232 (FAM)



Assay: Hs EGFR 4704-4789 (MAX)

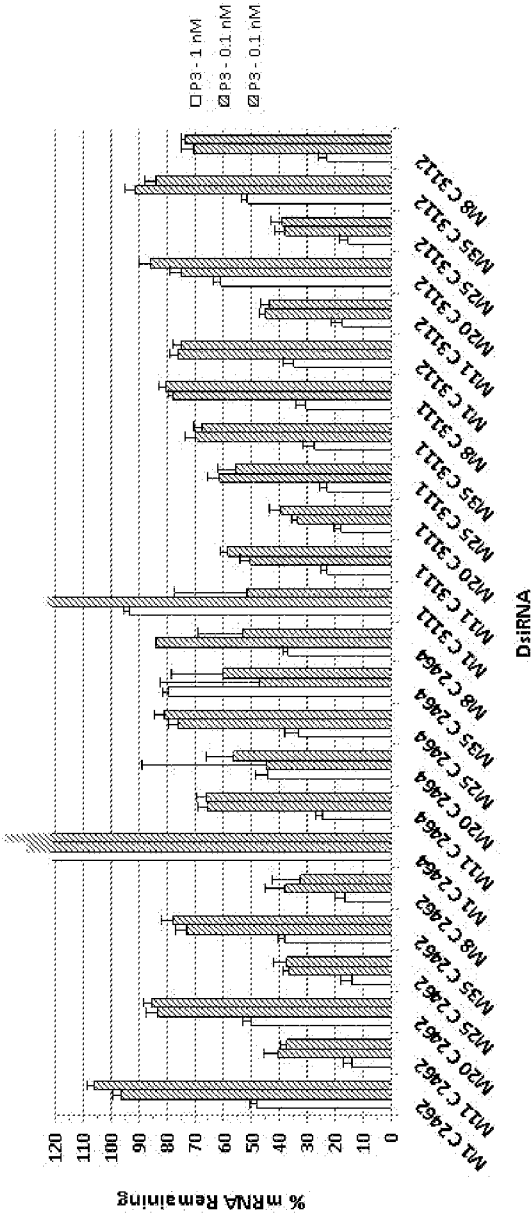
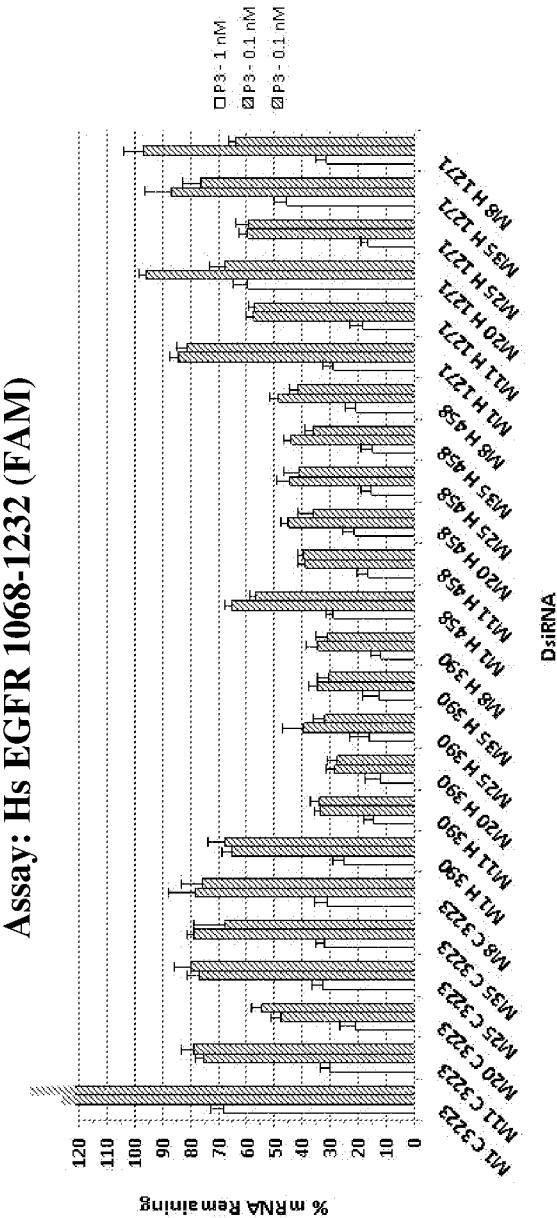


Figure 4D

Human EGFR Knockdown in Human HeLa Cells – Phase 3
Normalized to Hs HPRT 517-591 (FAM) and Hs SFRS9 569-712 (MAX) vs M8INC1, M8INC5, M8INC7
DsiRNAs: EGFR-3223, EGFR-390, EGFR-458, EGFR-1271



Assay: Hs EGFR 4704-4789 (MAX)

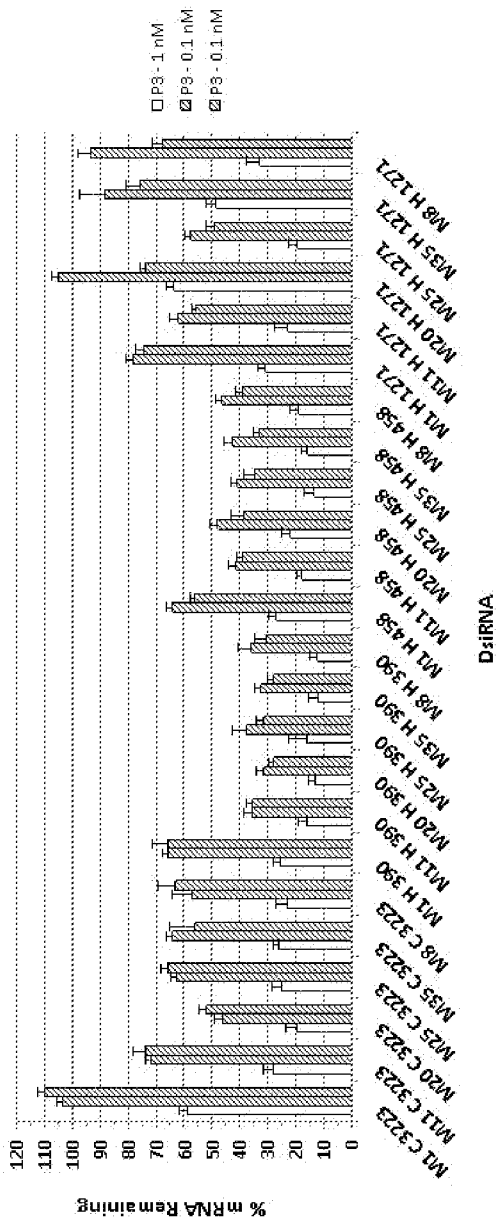
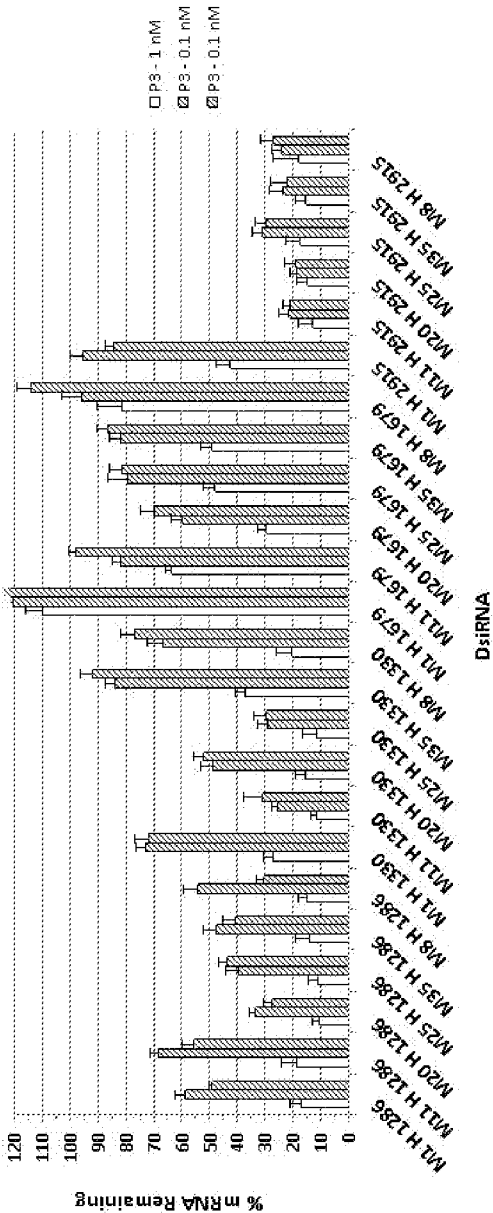


Figure 4E

Human EGFR Knockdown in Human HeLa Cells – Phase 3
Normalized to Hs HPRT 517-591 (FAM) and Hs SFRS9 569-712 (MAX) vs M8INC1, M8INC5, M8INC7
DsiRNAs: EGFR-1286, EGFR-1330, EGFR-1679, EGFR-1679, EGFR-2915

Assay: Hs EGFR 1068-1232 (FAM)



Assay: Hs EGFR 4704-4789 (MAX)

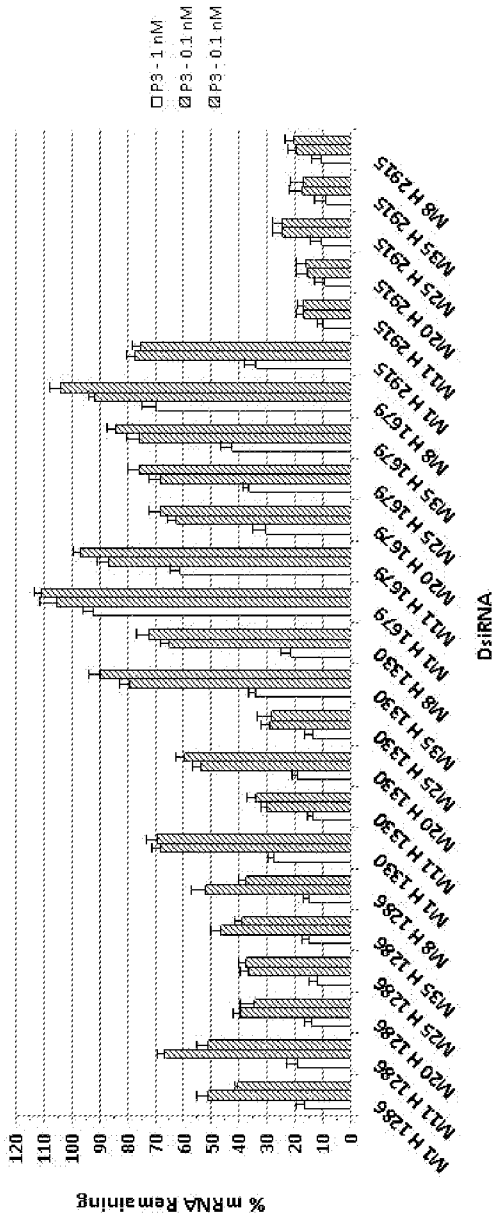
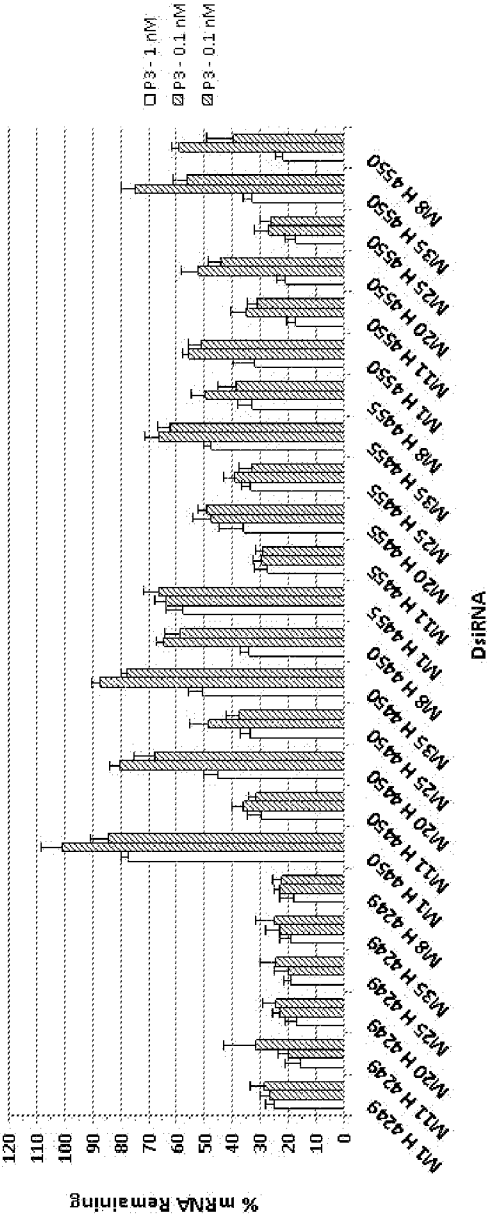


Figure 4F

Human EGFR Knockdown in Human HeLa Cells – Phase 3
Normalized to Hs HPRT 517-591 (FAM) and Hs SFRS9 569-712 (MAX) vs M8INC1, M8INC5, M8INC7
DsiRNAs: EGFR-4249, EGFR-4249, EGFR-4450, EGFR-4455, EGFR-4550

Assay: Hs EGFR 1068-1232 (FAM)



Assay: Hs EGFR 4704-4789 (MAX)

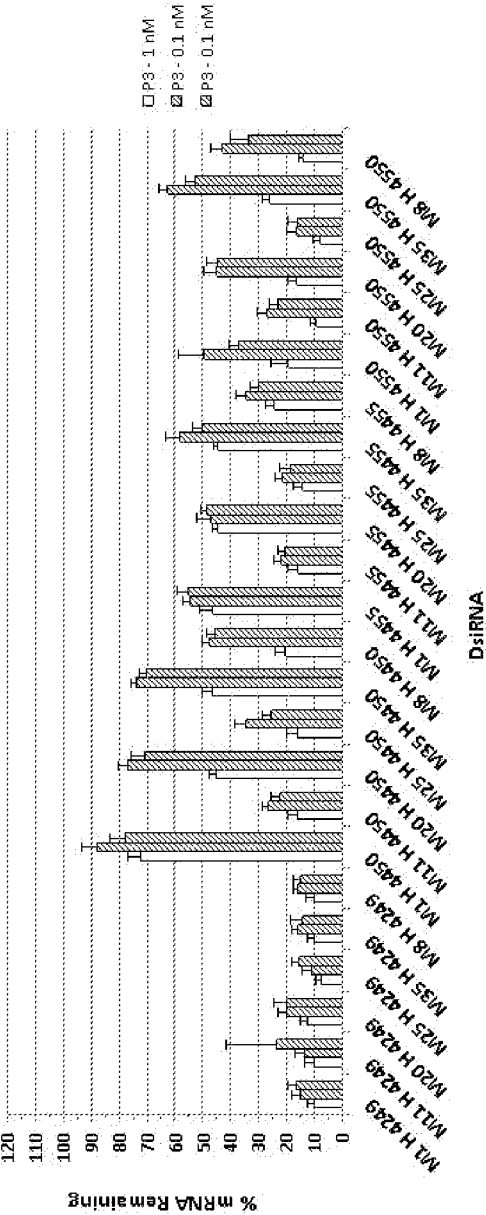
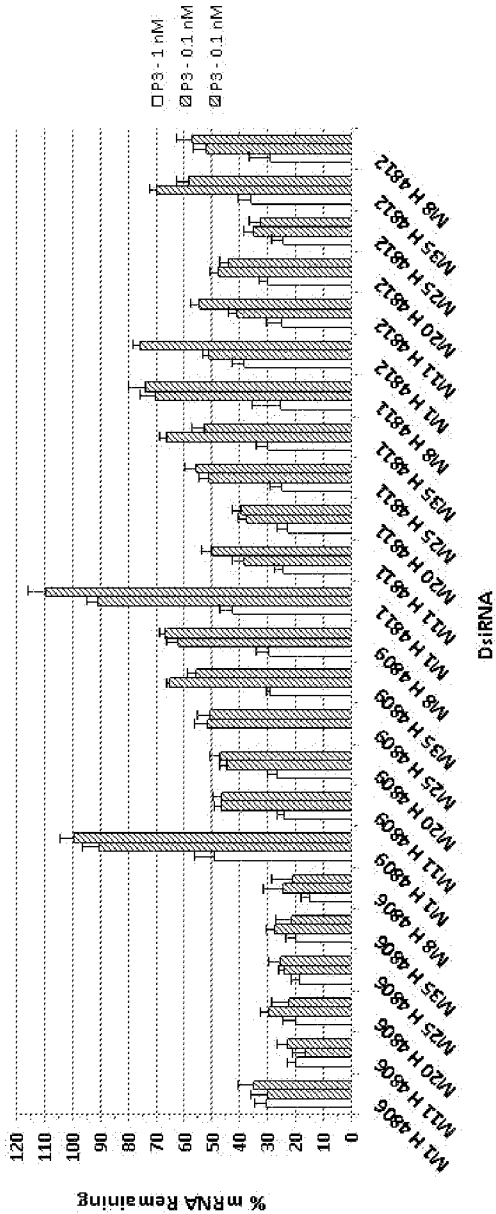


Figure 4G

Human EGFR Knockdown in Human HeLa Cells – Phase 3
Normalized to Hs HPRT 517-591 (FAM) and Hs SFRS9 569-712 (MAX) vs M8INC1, M8INC5, M8INC7
DsiRNAs: EGFR-4806, EGFR-4809, EGFR-4811, EGFR-4812

Assay: Hs EGFR 1068-1232 (FAM)



Assay: Hs EGFR 4704-4789 (MAX)

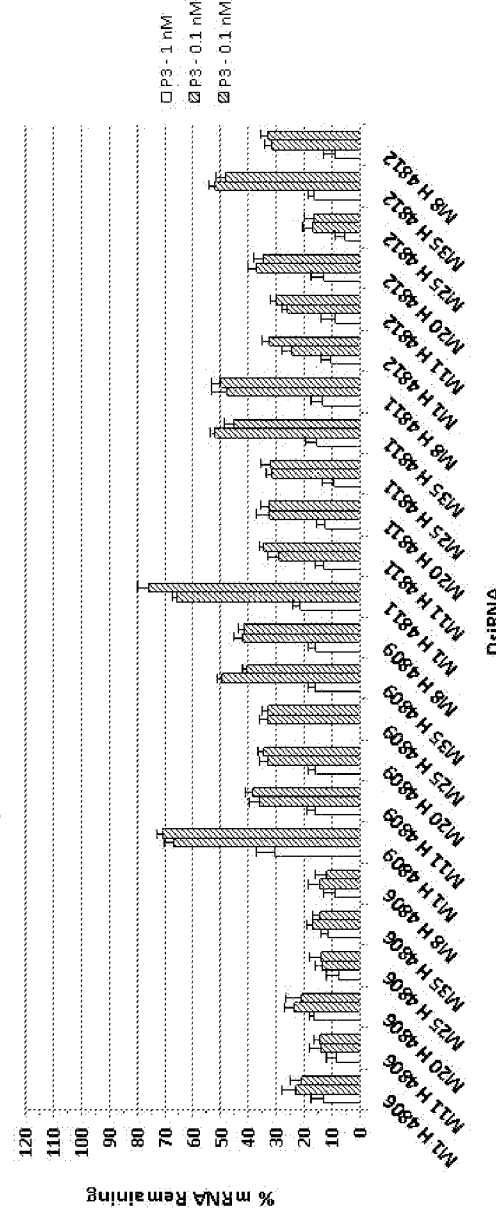
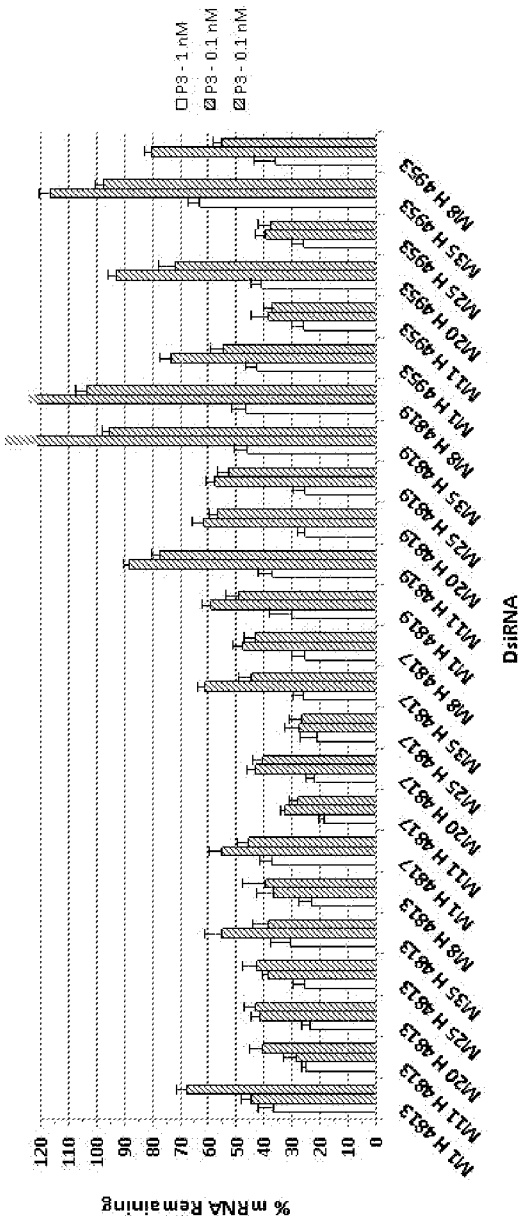


Figure 4H

Human EGFR Knockdown in Human HeLa Cells – Phase 3
Normalized to Hs HPRT 517-591 (FAM) and Hs SFRS9 569-712 (MAX) vs M8INC1, M8INC5, M8INC7
DsiRNAs: EGFR-4813, EGFR-4817, EGFR-4819, EGFR-4953

Assay: Hs EGFR 1068-1232 (FAM)



Assay: Hs EGFR 4704-4789 (MAX)

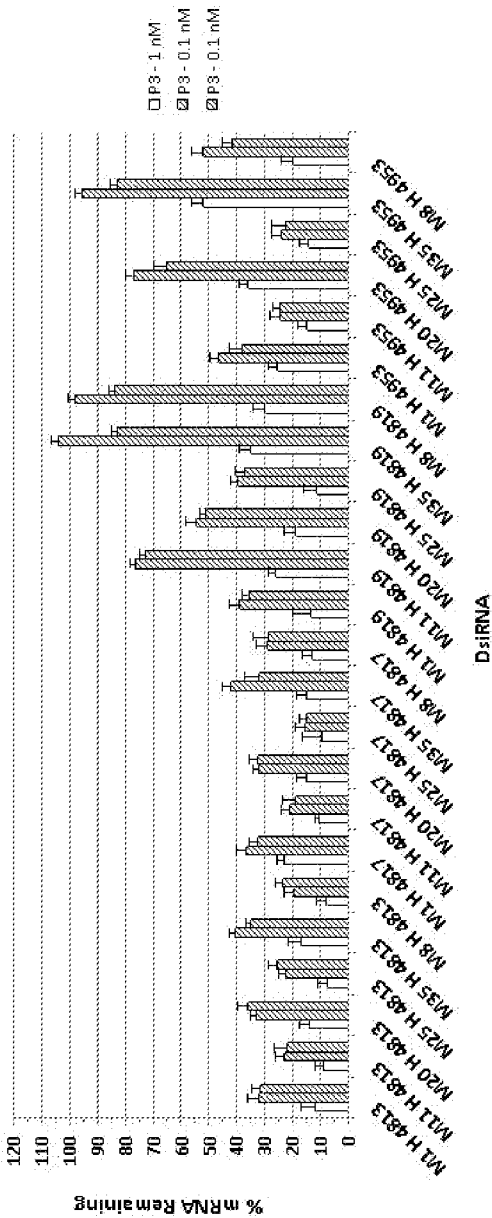
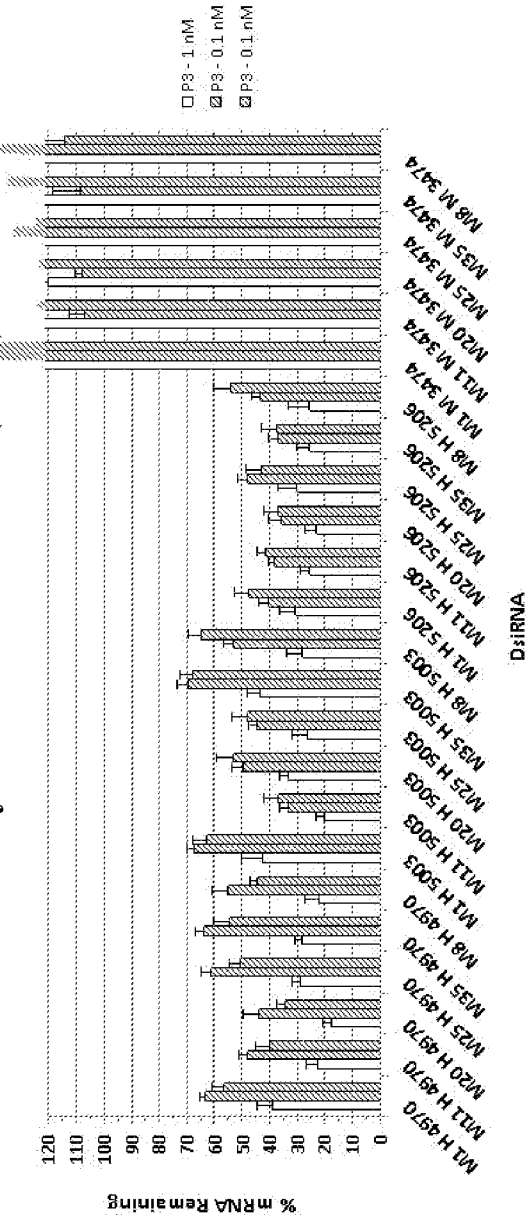


Figure 4I

Human EGFR Knockdown in Human HeLa Cells – Phase 3
Normalized to Hs HPRT 517-591 (FAM) and Hs SFRS9 569-712 (MAX) vs M8INC1, M8INC5, M8INC7
DsiRNAs: EGFR-4970, EGFR-5003, EGFR-5206, EGFR-m3474

Assay: Hs EGFR 1068-1232 (FAM)



Assay: Hs EGFR 4704-4789 (MAX)

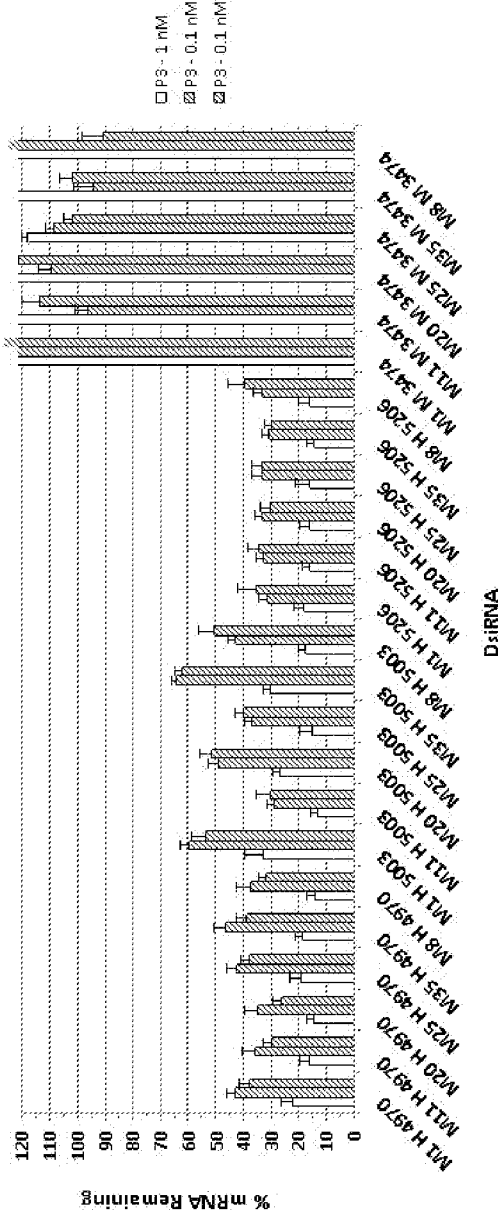


Figure 5

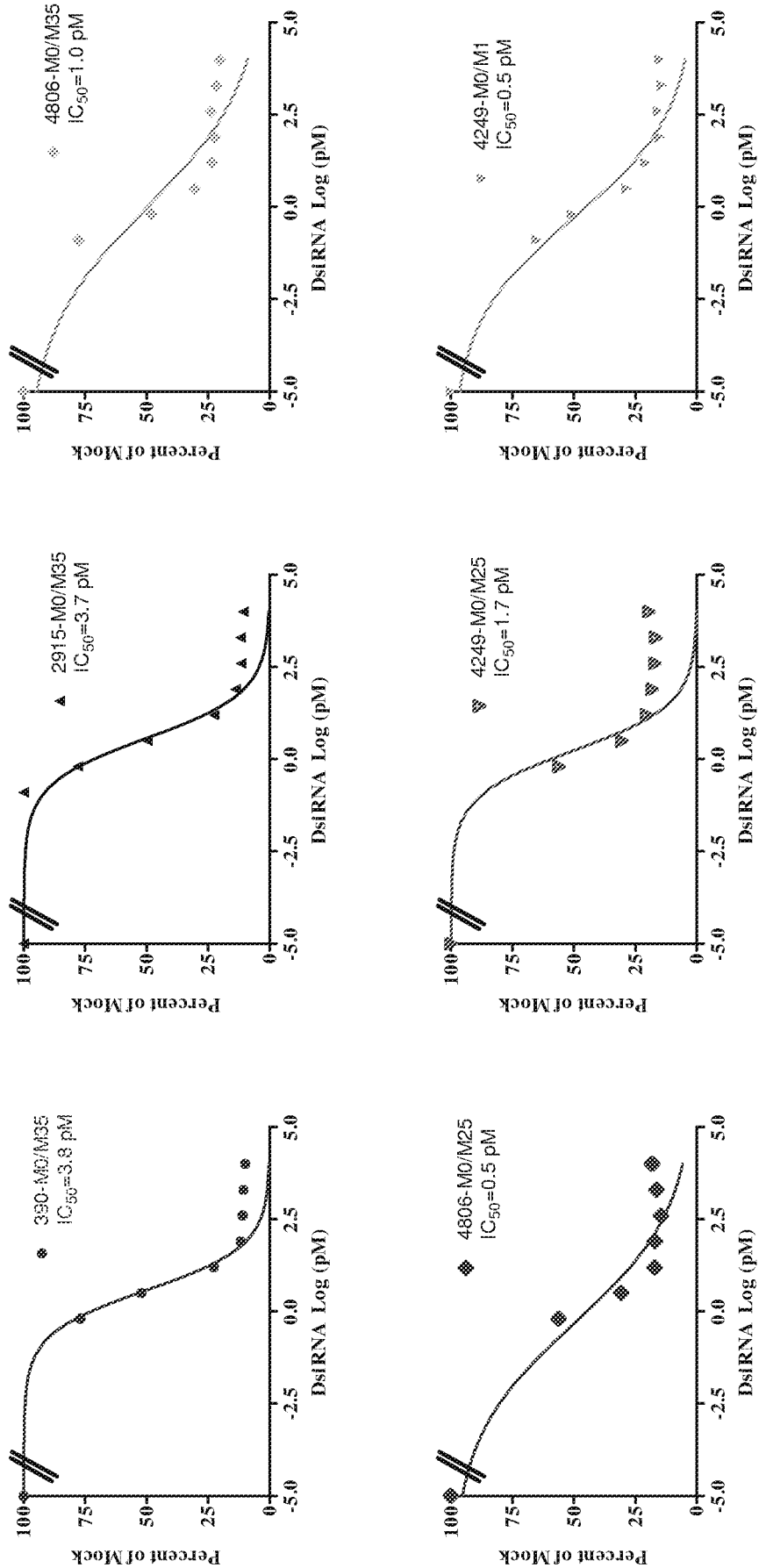


Figure 6

