

Methods for Analysis of Oligonucleotide Drugs

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Classical assays remain the foundation for characterizing antisense oligonucleotide (ASO) efficacy and safety, but their varied performance highlights both critical strengths and notable gaps. Absorption studies utilize liquid chromatography tandem mass spectrometry (LC-MS/MS)^{1,2} or ligand binding assays (LBA)^{3,4} to determine the concentration of ASOs in plasma, tissue homogenates, and other biofluids.⁵ Distribution studies utilize radiolabeling of the ASO⁶ or hybridization assays,^{7,8} such as *in situ* hybridization (ISH) or dual-ISH (DISH),⁹ and frequently rely on microscopy to visualize tissue distribution and intracellular localization. ASOs are often labeled with a fluorescent tag (e.g., Cy3), which has been reported to significantly alter cellular uptake and other pharmacodynamic properties of the drug.⁵ Metabolism and excretion studies, including those designed to detect metabolites of ASOs, utilize LC-MS/MS to detect drug in urine and other biofluids and may require the use of radiolabeling to isolate 3' or 5' "shortmer" sequences.^{4,5,7}

Bioanalytical methods rely on hybridization of the ASO to a complementary oligonucleotide sequence where subsequent ligation of a tagged probe sequence is detected using enzyme-labeled antibodies,¹⁰ or likewise in an electrochemiluminescent platform.¹¹ Variants of this method using branched DNA can increase sensitivity and accuracy.^{12,13} In addition, hybridization-ligation ELISA (HL-ELISA) and reverse-transcription quantitative polymerase chain reaction (RT-qPCR) have further improved the sensitivity of these assays and the ability to quantitate oligonucleotides.¹⁰ Quantitative PCR (qPCR) has the highest sensitivity for measuring and monitoring ASOs, whereas LC-MS/MS has the best specificity.¹⁴⁻¹⁷

Custom-made antibodies are often developed for specific ASOs, where the resultant antibody may recognize sequence, conformation, modification, and other possible epitopes. As such, these antibodies are typically generated and used "in-house" and may not have utility for other ASO drugs or across

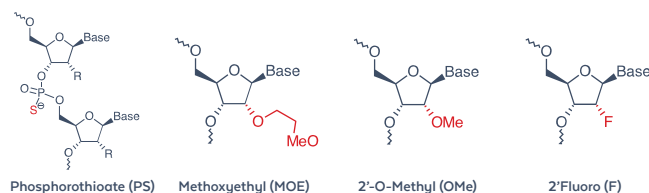


Figure 1. Structures of common chemical modifications to stabilize ASOs.

drug platforms. Additionally, they may not be available for use except by their originators, as gifts, or with limitations on use.^{18,19} By example, the antibody raised against the 20-mer PS ASO ISIS 2105 was designed to target human papilloma virus to detect ASOs containing PS bonds, but does not have any specificity to second-generation modifications.²⁰

With well-established pros and cons,²¹ these classical assays are strongly influenced by the length, sequence, and chemical modifications of the target oligonucleotide. Many suffer from a "general lack of sensitivity" needed for preclinical assays, creating an unmet need for alternatives.¹⁰ To address this, we developed monoclonal antibody reagents targeting nucleic acid backbones or sugar modifications, independent of sequence,²² with each panel specific to a defined chemical modification (see Figure 1).

	Antisense Oligo (ASO)	Messenger RNA (mRNA)	Small Interfering RNA (siRNA)
FDA Drugs	10+	2+	6+
Mechanism	Hybridizes with target RNA to modulate splicing or suppress expression	Delivers a genetic blueprint to the cytoplasm for translation	Enters the RISC complex to cleave target mRNA
Impact	Can silence, correct, or fine-tune protein output	Boosts or restores protein production	Potent, highly selective silencing of disease-driving proteins
Strength	Precision control, including splice correction	Flexible platform: vaccines, enzymes, antibodies	Excellent specificity, long-lasting action, infrequent dosing
Limitation	Potential off-target binding and toxicity	Requires stabilization and ultra-cold storage	Delivery to diverse tissues remains a hurdle

Figure 2. ASO, siRNA & mRNA: impact, strengths & weaknesses.

These antibodies provide sensitive and versatile tools for visualization, quantification, and detection in immunocytochemistry (ICC), ELISA, immunohistochemistry (IHC), and other standard immunoassays. They detect panels of ASO, siRNA, and mRNA with differing sequences yet common chemical modifications (see Figure 2) and can be used either individually or in multiplexed formats, following the protocols detailed in this guide.

2D Cell Culture ASO Dosing

Culture cells, by example HeLa cells, in Dulbecco's modified Eagle's medium (DMEM) with GlutaMAX (Gibco) supplemented with 10% fetal bovine serum (FBS) (Rockland, #[FBS-01-0100](#)) and 1% penicillin-streptomycin (Gibco). For ICC, seed cells in 8-well chamber slides, either Millicell EZ SLIDE 8-well glass (Millipore) or Nunc Lab-Tek Chamber Slide Systems (Thermo Scientific) at a density of 17,000 cells in 400 μ L per well. Perform gymnotic delivery of ASOs by adding the ASO at between 100 nM to 10 μ M concentrations (optimum dose may be dependent on ASO) directly to the cell growth media before adding to the cells. Lipofection delivery was performed by diluting 1-2 μ L of Lipofectamine 2000 (Invitrogen) per well in Opti-MEM reduced serum medium (Gibco) to achieve 1:10 of the final volume, and then incubation for 5 minutes at room temperature. After incubation, diluted Lipofectamine was added to the diluted ASO in equal volume and incubated for 15 minutes, followed by addition of growth media to the desired final volume. Growth medium was replaced by the diluted Lipofectamine and ASO medium and incubated for 72 hours. ASOs obtained from IDT (*Integrated DNA Technologies*) were synthesized and purified using HPLC.

2D Cell Culture ICC

Grow cells in cell chamber slides or on cover slips. Fix cells in 4% paraformaldehyde (PFA) in 1X phosphate-buffered saline (PBS) (Rockland, #[MB-008](#)) for 15 to 20 minutes at room temperature. After incubation, wash cells twice with 1X PBS and once with PBS-T (1X PBS with 0.01% TWEEN-20 (Rockland, #[MB-075-1000](#)) or Triton X-100 for 5 minutes. Block cells using 5% goat serum (Rockland, #[B304](#)) in 1X PBS-T for 60 minutes at room temperature. Add primary monoclonal antibody of ModDetect™ anti-PS (see page 5 for ordering information) diluted in same blocking buffer at 1:1,000 dilution and incubate for 120 minutes at room temperature. If multiplexing, additional primary antibodies, for instance a 1:250 dilution of rabbit anti-alpha tubulin (Rockland, #[600-401-880](#)) may be added at this time (see table 2 for additional antibodies to subcellular markers). After primary antibody incubation, wash cells 3 times with PBS-T and then add the required secondary antibodies; 1:2,000 dilution of goat anti-mouse IgG pre-adsorbed Dylight™ 488 (Rockland, #[610-141-121](#)) and any other required secondary antibody, for example a 1:2,000 dilution of goat anti-rabbit IgG pre-adsorbed Dylight™ 549 (Rockland, #[611-142-122](#)) to detect rabbit anti-alpha tubulin. When multiplexing, always carefully select secondary antibodies to ensure no unwanted cross reactivity with multiple primary antibodies. Incubate secondary antibodies for 1 hour at room temperature, followed by two PBS-T and one with 1X PBS wash for 5 minutes each. Counterstain nuclei with 40,6-diamidino-2-phenylindole (DAPI) or Hoechst 33342 as directed by the manufacturer and mount with Fluoromount-G mounting medium (Thermo Fisher). Image slides using a confocal microscope under the proper conditions for multiplex detection, image processing, and data analysis.

Anti-PS ELISA

Synthesize oligonucleotide with more than one PS bond. The signal may be proportional to the total number of PS bonds present within the ASO. More than one PS bond is required so that capture and detection antibodies used in the sandwich ELISA do not compete and/or are not blocked by steric hindrance. Coat 96-well plates with one of three ModDetect™ antibody clones (Rockland, PS03: #[200-301-MU9](#); PS04: #[200-301-MV0](#); PS05: #[200-301-MV1](#)) at 2 μ g/mL in 0.1M sodium bicarbonate pH 9.5 and incubate overnight at 4°C. Wash three times with PBS-T (Rockland, #[MB-075-1000](#)), and then add 300 μ L of ELISA Microwell blocking buffer (Rockland, #[MB-064-0100](#)) for 2 hours at room temperature. Prepare ASO at 100 ng/mL in sample buffer (Rockland, #[MB-070](#)). Add 100 μ L to each well in triplicates, followed by incubation for 2 hours at room temperature with agitation at 450 RPM. After three PBS-T washes, add 100 μ L of a biotinylated version of the same ModDetect antibody panel (Rockland, PS03: #[200-306-MU9](#); PS04: #[200-306-MV0](#); PS05: #[200-306-MV1](#)) prepared at 0.5 μ g/mL and added to the appropriate wells for 1 hour at room temperature with agitation at 450 RPM. After three further PBS-T washes, add 100 μ L of streptavidin-HRP (Rockland, #[S000-03](#)) at 0.125 μ g/mL in sample buffer to each well for 30 minutes at room temperature with agitation at 450 RPM. After three additional PBS-T washes, add 100 μ L of 3,3',5,5'-tetramethylbenzidine (Rockland, #[TMBE-100](#)) and incubate for 30 minutes at room temperature in the dark. Stop the reaction by adding 100 μ L of 1N HCl to each well and read the absorbance at 450-630 nm within 5 minutes.

Table 1. Comparison to other methods utilized for the quantification of ASOs

	ModDetect™ ELISA	LC-MS	hELISA	Branched DNA	qPCR
Sensitivity	~ 1 pM	~100 pM ^[5]	~10 pM ^[6]	~1 pM ^[7]	~1 pM ^[8]
Cost	\$	\$\$\$\$	\$-\$	\$	\$
Throughput	●	●	●	●	●
Complexity	Sequence independent + Universal capture based on modification	Requires intensive sample preparation, expensive instrumentation, and skilled operators	Requires additional hybridization and incubation steps + Customized probes	Requires multiple hybridization and signal amplification steps + Customized probes	Requires nucleic acid extraction, primer/probe design, and precise thermal cycling + Customized probes

Anti-MOE ELISA

Synthesize oligonucleotide with more than one MOE-modified base. As for PS, for MOE detection the signal may be proportional to the total number of MOE bonds present within the ASO. This protocol specifies conditions for an indirect ELISA with the antigen bound to the plate. By example, coat 96-well plates with a bovine serum albumin conjugated (to facilitate binding to the plate) 20-mer 5'-10-5 gapmer containing 20-MOE-modified bases in the wings, DNA in the gap, and all PS bonds diluted to 5 µg/mL in 0.05M sodium bicarbonate buffer pH 9.5. Add 100 µL of diluted antigen to each well and incubate at 4°C for 16-18 hours. Remove excess antigen and wash the plate three times with 1X PBS (Rockland, #[MB-008](#)). Block the plate using 3% fish gel (Sigma, #G7765) or for best results use ELISA Microwell blocking buffer (Rockland, #[MB-064-0100](#)) at room temperature for 1 hour and then remove excess blocking solution. Next add primary antibody as 3-fold serial dilutions at room temperature for 1 hour using ModDetect™ anti-2'MOE antibody clones (MOE1: Rockland, #[200-301-NF0](#); MOE3: #[200-301-NF1](#); MOE4: #[200-301-NF2](#); MOE9: #[200-301-NF9](#); and MOEC: #[200-301-NF4](#)) (see page 5 for ordering information) to determine which clone reacts best to the applied antigen. Remove excess antibody from the plate was washed three times with PBS-T (Rockland, #[MB-075-1000](#)). Next add 100 µL to each well of a 1:8,000 dilution of secondary antibody rabbit anti-mouse IgG HRP (Rockland, #[610-403-C46](#)) prepared in 1% fish gel solution in 1X PBS. Allow binding at room temperature for 1 hour. Remove excess conjugate and wash the plate three times with PBS-T. Add 100 µL of TMB substrate solution (Rockland, #[TMBE-100](#)) at room temperature for 30 minutes and read the absorbance at 450 nm within 5 minutes.

3D Spheroid/Organoid Culture ASO Dosing

Culture cells, by example SH-SY5Y cells, a neuroblastoma cell line derived from a metastatic bone tumor, in T75 flasks with tissue culture treatment surfaces (NUNC) in Dulbecco's modified Eagle's medium (DMEM) supplemented with 10% fetal bovine serum (FBS) (Rockland #[FBS-01-0100](#)). When cells reached the exponential growth phase, detach cells with TrypLE (Thermo Fisher) and resuspended in ultralow-adherence U-bottom 96-well plates (Corning), at a density of 10,000 cells per well. After 4 days of spheroid formation for gymnotic delivery add ASO between 100 nM to 10 µM concentrations (optimum dose may be dependent on ASO23) directly to the cell culture medium for an additional 3 to 7 days of incubation. For transfection, prepare an ASO-Lipofectamine 2000 (Invitrogen) complex incubating 3 µL per well of Lipofectamine with the ASO at room temperature for 15 minutes. Remove the culture medium from the spheroids and then 50 µL of Accutase Cell Dissociation Reagent (Thermo Fisher) into each well and then return to the 37°C incubator for an additional 15 minutes. After incubation, the spheroids were homogenized by pipetting up and down five times. Gently centrifuge cells at 300g for 5 minutes and remove the supernatant. Proceed with 3D cell culture ICC.

3D Cell Culture ICC

Fix spheroids in 4% paraformaldehyde (PFA) in 1X phosphate-buffered saline (PBS) (Rockland, #[MB-008](#)) for 30 minutes at room temperature and then washed twice in 1X PBS. Block spheroids in 10% goat serum (Rockland, #[B304](#)) in 1X PBS supplemented with 0.1% Tween-20 (PBS-T) (Rockland, #[MB-075-1000](#)) for 45 minutes. Dilute primary antibody, by example a 1:1,000 dilution of the ModDetect™ anti-PS clone PS03 (Rockland, #[200-301-MU9](#)) in 1X PBS. Additional antibodies to subcellular markers may be added, if desired. After overnight incubation of the primary antibody at 4°C, wash the spheroids with 1X PBS at room temperature twice for 15 minutes each. Next add a 1:1,000 dilution in 1X PBS of secondary antibody rabbit anti-mouse IgG DL488 (Rockland, #[610-441-C46](#)) and incubate for 90 minutes at room temperature. Wash the spheroids with 1X PBS twice for 15 minutes each and then once in deionized water. Counterstain nuclei with 40,6-diamidino-2-phenylindole (DAPI) or Hoechst 33342 as directed by the manufacturer and mount with Fluoromount-G mounting medium (Thermo Fisher). Image slides using a confocal microscope under the proper conditions for multiplex detection, image processing, and data analysis.

In Vivo ASO Dosing

Conduct all animal experiments according to established guidelines for the use and care of animals and obtain all required approvals for ethical use. By example, adult male C57BL/6JH strain mice may be used. Standard protocols to house mice, for instance, in individually ventilated cages in a pathogen-free environment, in a 12-hour light/12-hour dark cycle, with ad libitum access to standard rodent chow and water are recommended. Dilute the ASO in sterile 1X PBS to a final dose of 50 mg/kg and deliver subcutaneously to mice. Control animals were dosed with 1X PBS only. Harvest tissue 72 hours later for Tissue IHC.

Tissue IHC

Immerse ASO dosed mouse tissues in 10% neutral buffered formalin and fix for 30 hours and then process into wax blocks. Sections should be cut at 8 µm and mounted on Trubond™ 380 Adhesion slides (Electron Microscopy Sciences, #50-340-33) and dried overnight. Perform immunostaining using the M.O.M.® (Mouse on Mouse) Immunodetection Kit, Fluorescein (VectorLabs, #FMK-2201) as recommended by the manufacturer. Briefly, after dewaxing in xylene and rehydration into water followed by 1X PBS (Rockland, #[MB-008](#)), slides were blocked for 1 hour at room temperature followed by overnight incubation with ModDetect™ anti-PS clone PS03 (Rockland, #[200-301-MU9](#)) at a dilution of 1:1,000 in M.O.M. diluent (VectorLabs) at 4°C overnight. After two 1X PBS washes for 3 minutes each, add a 1:1,000 dilution in 1X PBS of secondary antibody rabbit anti-mouse IgG Biotin (Rockland, #[610-406-C46](#)) or the biotinylated anti-mouse IgG secondary antibody provided in the M.O.M.® kit (VectorLabs) and incubate for 1 hour at room temperature.

Wash slides twice for 3 minutes each with 1X PBS, followed by the addition of Streptavidin DL488 (Rockland, #[S000-41](#)) for 1 hour at room temperature. After two final 1X PBS washes of 3 minutes each, counterstain nuclei with 40,6-diamidino-2-phenylindole (DAPI) or Hoechst 33342 as directed by the manufacturer and mount with Fluoromount-G mounting medium (Thermo Fisher). Image slides using a confocal microscope under the proper conditions for multiplex detection (reference), image processing, and data analysis. Tissue IHC can be performed using anti-PS or anti-MOE mAbs.

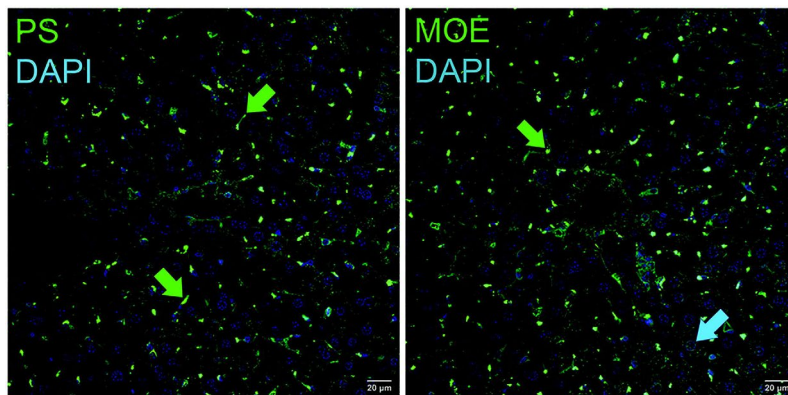


Figure 3. Biodistribution (IHC). Anti-PS antibody (clone PS03) and anti-MOE antibody (clone MOE4) detection of a 2'-MOE modified ASO 5-10-5 gapmer containing ten PS bonds delivered subcutaneously to mice (50 mg/kg, 72h). Liver tissue was immunostained with anti-PS or anti-MOE antibodies (green) diluted 1:1,000 (overnight) and counterstained with DAPI (blue). Representative positive immunostaining indicates accumulation of the ASO in non-parenchymal cells surrounding hepatocytes (green arrows). Large hepatocyte nuclei are indicated by blue arrows. PBS-treated mice (negative control) showed no reaction (data not shown). Scale bar is indicated.

ModDetect™ Ordering Information

ModDetect™ Anti-PS (Phosphorothioate) Clones

Product	Format	Item No.
Clone PS03	Unconjugated	200-301-MU9
Clone PS04		200-301-MV0
Clone PS05		200-301-MV1
Clone PS06		200-301-MW1
Clone PS07		200-301-MW0
Clone PS08		200-301-MV2
Clone PS09		200-301-MW3
Biotin Clone PS03	Biotin	200-306-MU9
Biotin Clone PS04		200-306-MV0
Biotin Clone PS05		200-306-MV1
Biotin Clone PS06		200-306-MW1
Biotin Clone PS07		200-306-MW0
Biotin Clone PS08		200-306-MV2
Biotin Clone PS09		200-306-MW3
DyLight™ 488 Clone PS03	DL488	200-341-MU9
DyLight™ 488 Clone PS04		200-341-MV0
DyLight™ 488 Clone PS05		200-341-MV1
DyLight™ 488 Clone PS06		200-341-MW1
DyLight™ 488 Clone PS07		200-341-MW0
DyLight™ 488 Clone PS08		200-341-MV2
DyLight™ 488 Clone PS09		200-341-MW3
DyLight™ 549 Clone PS01	DL549	200-342-MU7
DyLight™ 549 Clone PS02		200-342-MU8
DyLight™ 549 Clone PS03		200-342-MU9
DyLight™ 549 Clone PS04		200-342-MV0
DyLight™ 549 Clone PS05		200-342-MV1
DyLight™ 549 Clone PS06		200-342-MW1
DyLight™ 549 Clone PS07		200-342-MW0
DyLight™ 549 Clone PS08		200-342-MV2
DyLight™ 549 Clone PS09		200-342-MW3

ModDetect™ Anti-MOE (2'-O-Methoxyethyl) Clones

Product	Format	Item No.
Clone MOE1	Unconjugated	200-301-NF0
Clone MOE3		200-301-NF1
Clone MOE4		200-301-NF2
Clone MOE9		200-301-NF3
Clone MOEC		200-301-NF4
Biotin Clone MOE1	Biotin	200-306-NF0
Biotin Clone MOE3		200-306-NF1
Biotin Clone MOE4		200-306-NF2
Biotin Clone MOE9		200-306-NF3
Biotin Clone MOEC		200-306-NF4

ModDetect™ Anti-OME (2'-O-Methyl) Clones

Product	Format	Item No.
Clone OME1	Unconjugated	200-301-NF5
Clone OME2		200-301-NF6
Clone OME3		200-301-NF7
Clone OME4		200-301-NF8
Clone OME5		200-301-NF9

ModDetect™ Panels

Product	Format	Item No.
PS Panel	Unconjugated	KNA-100
PS Biotinylated Panel	Biotin	KNA-101
2'MOE Panel	Unconjugated	KNA-200
2'MOE Biotinylated Panel	Biotin	KNA-201
2'OMe Panel	Unconjugated	KNA-300

Antibodies to Subcellular Markers for Multiplex Detection with ModDetect™

Lysosome Markers

Product	Item No.
Cathepsin L (AA114-288) Antibody	ABIN7431587
CTSA (N-Term) Antibody	ABIN654433
Cathepsin D (C-Term) Antibody	ABIN6254162
LAMP1 (AA 80-280) Antibody	ABIN3016286
Cathepsin K (AA 54-317) Antibody	ABIN7441856
Cathepsin S (AA 115-331) Antibody	ABIN7434368
Cathepsin D (AA 66-410) Antibody	ABIN7433375
LAMP2 (AA 191-362) Antibody	ABIN7437248
LAMP1 (AA 301-417) Antibody	ABIN676088
Cathepsin L (AA 71-170)	ABIN687532
LAMP2 (AA 29-169) Antibody	ABIN5611243

Endosome Markers

Product	Item No.
EEA1 (RABBIT) Antibody	ABIN521882
RAB7B (AA 100-199) Antibody	ABIN567027
RAB5 (C-Term) Antibody	ABIN361846
RAB5B (C-Term) Antibody	ABIN1439995
RAB5C (C-Term) Antibody	ABIN6254194
RAB7A (C-Term) Antibody	ABIN720191
RAB9A (RABBIT) Antibody	ABIN564041

Cytoskeleton Markers

Product	Item No.
Vimentin (AA 371-466) Antibody	ABIN672786
Alpha Tubulin Antibody	ABIN93891
TUBB Antibody	ABIN93914
Smooth Muscle Actin (N-Term) Antibody	ABIN6254917
ACTC1 Antibody	ABIN2855212
ACTN2 Antibody	ABIN2855582
ACTG2 (AAA 3-376) Antibody	ABIN7440569
Myosin (AA 1069-1331) Antibody	ABIN7439273
Alpha Actinin Antibody	ABIN7073023
Dystrophin (AA 346-635) Antibody	ABIN1679546
ACTN3 (N-Term) Antibody	ABIN6258681
Cytokeratin 8/18 Antibody	ABIN285686

3D Cell Culture Products

3D Cell Culture Products

Product	Item No.
Rat Tail Type I Collagen-coated T-75 Flask	KOA-FMF8
Rat Tail Type I Collagen-coated 96-well Multiwell Plate	KOA-PMF8
Ultrapure Collagen I for Plate Coating - Bovine Placenta	001-G70-MF0
Ultrapure Collagen I for Tissue Engineering - Bovine Placenta	001-G70-MF1
Collagen I for Plate Coating - Bovine Skin	001-G70-MF6
Ultrapure Collagen III for Tissue Engineering - Bovine Placenta	001-G70-MF3
Ultrapure Collagen I for Plate Coating - Human Placenta	009-G70-MF0
Fetal Bovine Serum	FBS-02-0050
Fetal Bovine Serum, Certified, Heat Inactivated	FBS-01-0100

Lab Favorites

Epitope Tags

Product	Item No.
Antibody for the detection of DYKDDDDK (FLAG™)	200-301-383
Beta Galactosidase Antibody	200-4136-0100
6X His Epitope Tag Antibody	200-301-382
GFP Antibody	600-101-215
GFP Monoclonal Antibody	600-301-215
GST Antibody	600-101-200
GST Antibody Biotin Conjugated	600-106-200
HA Epitope Tag Antibody	600-401-384
RFP Antibody	600-901-379
RFP Antibody Pre-adsorbed	600-401-379
RFP Antibody Biotin Conjugated Pre-adsorbed	600-406-379

TrueBlot for IP/Western Blot

Product	Item No.
Mouse TrueBlot® ULTRA: Anti-Mouse Ig HRP	18-8817-33
Rabbit TrueBlot®: Anti-Rabbit IgG HRP	18-8816-31
TrueBlot® Anti-Rabbit Ig IP Agarose Bead	00-8800-25

Supporting Reagents

Product	Item No.
10X TTBS pH 7.5	MB-013
Blocking Buffer for Fluorescent Western Blotting	MB-070
Bovine Serum Albumin - Fraction V	BSA-50
Bovine Serum Albumin 30% Solution	BSA-30
Chemiluminescent FemtoMax™ Super Sensitive HRP Substrate	FEMTOMAX-110
ELISA Microwell Blocking Buffer with Stabilizer (Azide and Mercury Free)	MB-064-1000
Molecular Biology Grade UltraPure Water	MB-010-1000
STREPTAVIDIN	S000-01
STREPTAVIDIN ATTO 532 Conjugated	S000-53
STREPTAVIDIN PEROXIDASE Conjugated	S000-03
TMB ELISA PEROXIDASE SUBSTRATE	TMBE-1000
UltraPure Sterile Water	MB-009-1000

Oligonucleotide Drugs, Disease Areas, and Antibodies to the Target

Clinical Name	Target Protein	Disease State/Area of Interest	Item No.
Aganirsen	Insulin Receptor Substrate-1 (IRS-1)	Keratitis, Wet Age-Related Macular Degeneration (AMD)	600-401-445
Alicaforsen	Intercellular Adhesion Molecule 1 (ICAM-1)	Inflammation, Inflammatory Bowel Disease (IBD)	Various
Apatorsen	Heat Shock Protein 27 (Hsp27)	Oncology	Various
Aprinocarsen	Protein Kinase C Alpha (PKCα)	Chemotherapy	Various
ASO 556089	Metastasis-Associated Lung Adenocarcinoma Transcript 1 (MALAT1)	Oncology	Various
Atesidorsen	Growth Hormone Receptor (GHR)	Acromegaly	Various
Baliforsen	Myotonic Dystrophy Protein Kinase (DMPK)	Myotonic Dystrophy (DM)	Various
Bepirovirsen	Hepatitis B Virus (HBV) Sequence	Hepatitis B Virus (HBV)	Various
Casimersen	Dystrophin Protein (Exon 45)	Duchenne Muscular Dystrophy (DMD)	Various
Cavrotolimod	Toll-Like Receptor 9 (TLR9) Agonist	Oncology	Various
Cepadacursen	Proprotein Convertase Subtilisin/Kexin Type 9 (PCSK9)	Hypercholesterolemia	Various
Cobomarsen	JAK/STAT, MAPK/ERK, PI3K/AKT	B-Cell Lymphoma	Various
Custirsen	Clusterin (CLU)	Oncology / Chemotherapy	Various
Danvatirsen	Signal Transducer and Activator of Transcription 3 (STAT3)	Tumor Cell Growth	Various
Drisapersen	Dystrophin Protein (Exon 51)	Duchenne Muscular Dystrophy (DMD)	Various
Eplontersen	Transthyretin (TTR)	Amyloid Transthyretin Amyloidosis (ATTR)	200-901-FM9
Eteplirsen	Dystrophin Protein (Exon 51)	Duchenne Muscular Dystrophy (DMD)	Various
Fesomersen	Coagulation Factor XI (FXI)	Thrombosis	Various
Fomivirsen	Cytomegalovirus (CMV) Early Protein 2	Antiviral, Cytomegalovirus (CMV), Acquired Immunodeficiency Syndrome (AIDS)	Various
Golodirsen	Dystrophin Protein (Exon 51)	Duchenne Muscular Dystrophy (DMD)	Various
Inotersen	Transthyretin (TTR)	Transthyretin Amyloidosis (ATTR)	200-901-FM9
IONIS-FB-LRx	Complement Factor B (CFB)	Geographic Atrophy (GA)	Various
Ionis-MAPTRx	Tau Protein (MAPT)	Alzheimer's Disease (AD)	Various
ISIS 104838	Tumor Necrosis Factor Alpha (TNFα)	Inflammation / Arthritis	Various
ISIS 626112	Metastasis-Associated Lung Adenocarcinoma Transcript 1 (MALAT1)	Oncology	600-101-111
Mipomersen	Apolipoprotein B (ApoB)	Homozygous Familial Hypercholesterolemia (HoFH)	None
Monarsen	Acetylcholinesterase (AChE) / Acetylcholine Receptor (AChR)	Autoimmune Myasthenia Gravis (MG)	Various
Mongersen	Mothers Against Decapentaplegic Homolog 7 (SMAD7) / Transforming Growth Factor Beta 1 (TGFβ1)	Inflammation / Colitis	200-401-116
Nusinersen	Survival Motor Neuron Protein (SMN)	Survival Motor Neuron 2 Gene (SMN2)	Various
Oblimersen	B-Cell Lymphoma 2 (Bcl-2)	Oncology	200-401-Z43
Olaptesed pegol	C-X-C Motif Chemokine Ligand 12 (CXCL12)	Lymphocytic Leukemia	Various
Olezarsen	Apolipoprotein C-III (ApoC-III)	Hypercholesterolemia, Cardiovascular Disease (CVD)	600-101-114
Pelacarsen	Apolipoprotein A (ApoA)	Lipoprotein(a) (Lp(a)) Disorders / Liver Disease	600-401-Y42
Prexigebersen	Growth Factor Receptor-Bound Protein 2 (Grb2)	Oncology	Various
Rovanersen (WVE-120101)	Huntingtin Protein (HTT)	Huntington's Disease (HD)	Various
Rugonersen	Ubiquitin-Protein Ligase E3A (UBE3A)	Angelman Syndrome (AS)	Various
SPC5001	proprotein convertase subtilisin/kexin type 9 (PCSK9)	Hypercholesterolemia	Various
Tadnersen	C9ORF72 gene	Amyotrophic Lateral Sclerosis (ALS)	200-901-MH2
Tau ASO-12	Tau Protein (MAPT)	Alzheimer's Disease (AD)	Various
Tofersen	Superoxide Dismutase 1 (SOD1)	Amyotrophic Lateral Sclerosis (ALS)	Various
Tominersen	Huntingtin Protein (HTT)	Huntington's Disease	Various
Trabedersen	Transforming Growth Factor Beta 2 (TGFβ2) / SMAD	Brain / Solid tumors	Various
Trecovirsen	Human Immunodeficiency Virus (HIV) Gag Protein	Human Immunodeficiency Virus (HIV)	None
Ulefnersen	Fused in Sarcoma (FUS) Protein	Amyotrophic Lateral Sclerosis (ALS)	Various
Viltolarsen	Dystrophin Protein (Exon 53)	Duchenne Muscular Dystrophy (DMD)	Various
Volanesorsen	Apolipoprotein C-III (ApoC-III)	Familial Chylomicronemia Syndrome (FCS), Type 2 Diabetes (T2D), Hypertriglyceridemia	600-101-114
Vupanorsen	Angiopoietin-Like 3 (ANGPTL3)	Elevated Triglycerides and Atherogenic Lipoproteins	Various
Zilganersen	Glial Fibrillary Acidic Protein (GFAP)	Alexander disease (AxD)	200-301-W55
Zorevunersen	Sodium Voltage-Gated Channel Alpha Subunit 1 (SCN1A) / Nav1.1	Dravet Syndrome (DS)	200-301-G18

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