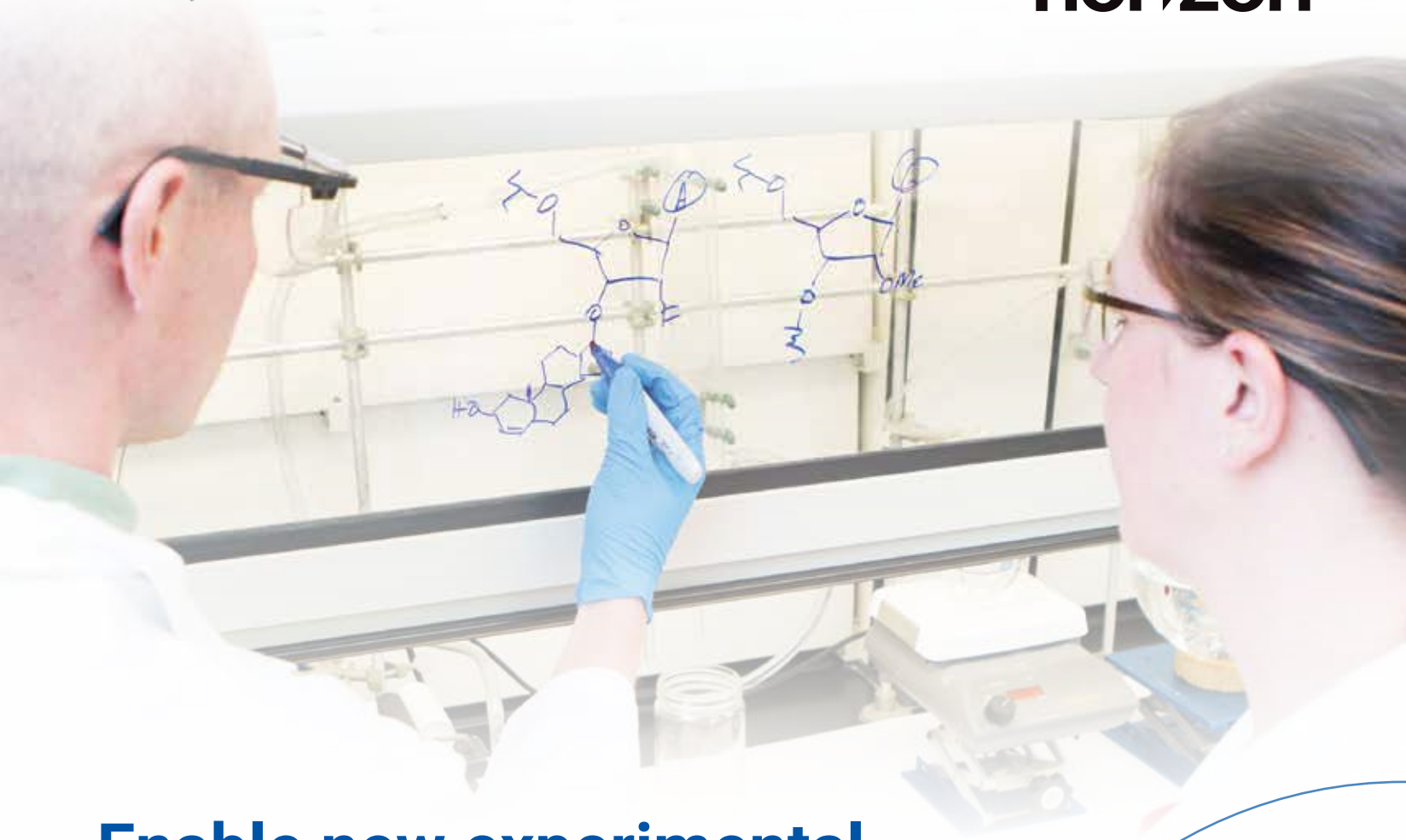
Dharmacon™ Reagents
Custom synthesis, RNAi, and CRISPR solutions

horizon



# Enable new experimental possibilities with custom RNA synthesis

Dharmacon™ custom RNA synthesis enables additional experimental abilities and scientific discoveries through unique chemistry, high quality, and dependable customer services.

- Benefits of 2'-ACE synthesis chemistry
- Extensive chemical modification options for RNA synthesis
- Long, high yield single strand RNA
- High performance siRNA with proprietary modifications
- "Have it your way" with post-synthesis options

# Improve delivery, stability, specificity and potency

We offer a wide array of chemical modifications for your custom RNA needs.

## Chemical Modification Options

- Base & backbone
- Labeling
- Modifiers
- Terminators

## More Synthesis Scales

We now offer all of our modifications at the 0.05 µmol synthesis scale. This reduced scale lends itself to lower costs, as well as a smaller amount of test material to run discovery projects. Also, we offer very large scale syntheses including delivery of gram quantities of RNA and DNA.

## Custom Amidites

We can produce custom amidites for your use or to incorporate into your RNA sequences of interest.

## We are here to help you

Every RNA molecule has unique synthesis challenges that vary by application, compatibility, sequence, length, and modification position. All of these factors contribute to the feasibility, yield, and purity of a custom synthesized RNA. You can rely upon our experts to aid your custom RNA designs and support your experimental goals.

We **GUARANTEE** more single-stranded RNA for your money.

### siRNA Bases and Modifications available

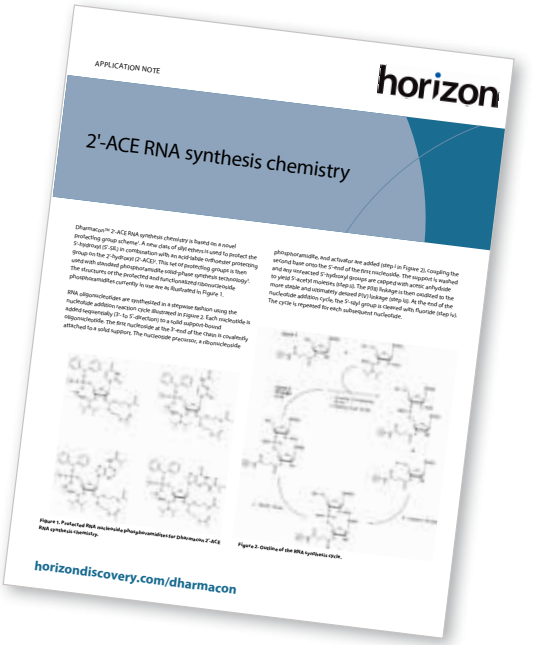
| Standard RNA Bases | Short Code |
|---|---|
| (A,C,G,U) | A,C,G,U |
| 2'-Omethyl RNA Bases | Short Code |
| 2'-OMe-(A,C,G,U) | mA,mC,mG,mU |
| Standard DNA Bases | Short Code |
| 2'-Deoxy-(A,C,G,T) | dA,dC, dG, dT |
| Base Modifications | Short Code |
| 1-Methyl-guanosine | m1G |
| 2,6-Diaminopurine | DAP |
| 2-Methyl-adenosine | m2A |
| 2-Aminopurine | 2AP |
| 4-Thio-uridine | 4-S-U |
| 5-Bromo-uridine | U[5Br] |
| 5-Fluoro-cytidine | C[5F] |
| 5-Fluoro-uridine | U[5F] |
| 5-Iodo-uridine | U[5I] |
| 5-Methyl-cytidine | 5-M-C |
| 5-Methyl-deoxycytidine | 5-M-dC |
| 5-Methyl-uridine | rT |
| Inosine | I |
| N2-Methyl-guanosine | m2G |
| N3-Methyl-uridine | 3-M-U |
| N6, N6-Dimethyl-adenosine | DMA |
| N6-Methyl-adenosine | m6A |
| Pseudo-uridine | ~U |
| Purine ribonucleoside | Pu |
| Pyrrolo-cytidine | pC |
| Ribavirin | RBV |

# 2’-ACE chemistry should be your synthesis standard

RNA applications can be performed with greater ease and confidence with the powerful advantages of the 2’-ACE technology.

- Greater reproducibility than any other chemistry
- Unmatched purity without additional purification time and expense
- Maximum sequence fidelity and integrity due to enhanced coupling efficiency

All synthetic RNA oligos must be chemically protected at multiple sites during synthesis, regardless of the chemistry platform used. However, 2’-ACE synthesis chemistry allows for the quickest and mildest deprotection conditions compared to other chemistries like 2’-tBDMS and “2’-TOM. Short deprotection times and a mild chemical environment promote the highest level of purity for synthetic RNA in the marketplace today.




**Download the App Note** 2’-ACE RNA Synthesis Chemistry for more information on the details of the RNA synthesis platform.

↘dharmacon.horizondiscovery.com/uploaded-Files/Resources/2-ace-rna-synth-chem-technote

## Advantage of Dharmacon 2’-ACE chemistry

| | **2'-ACE** | 2'-tBDMS | 2'-TOM |
|---|---|---|---|
| ASCE* | >99% | >98% | 95% |
| 21-mer ** | 81% | 65% | 34% |
| 50-mer ** | 61% | 36% | 8% |
| Coupling reaction | Fast | Slow | Slow |
| Deprotection conditions | Aqueous | Organic | Organic |
| Product can be delivered in 2'-protected or deprotected state | Yes | No | No |

*The average stepwise coupling efficiencies (ASCE) for each method.
**Percent full-length material listed above are approximate; exact yields will depend on sequence composition.

For unmodified, unpurified RNA, the above approximate percentages of full-length material can be expected.

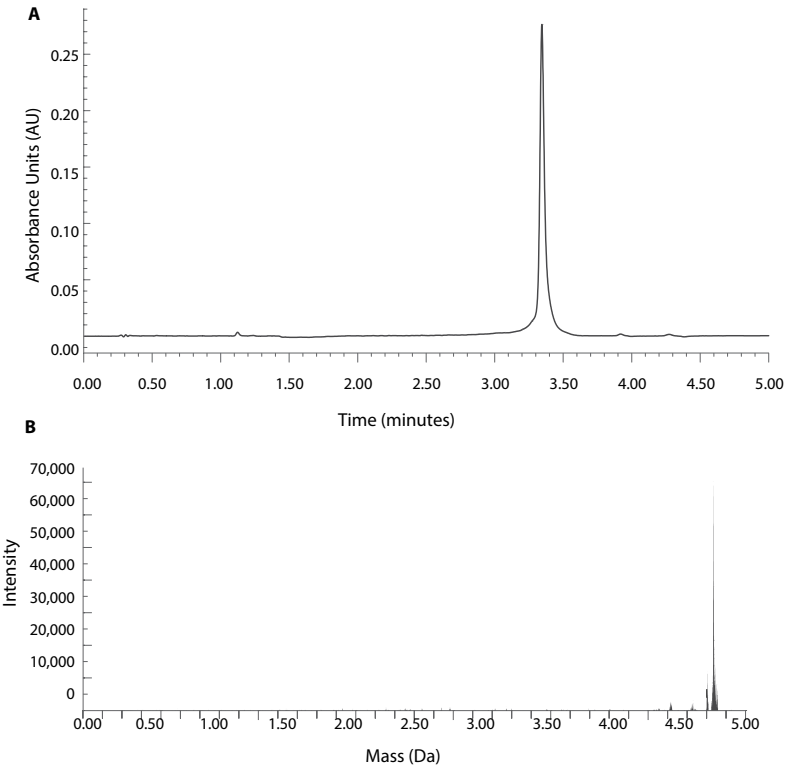
# When short RNAs just won't do

Long RNA molecules extend opportunities for RNA research and discovery. There are a multitude of uses for long RNA oligos including:

- Aptamers
- tRNAs
- Antisense technologies
- Ribozymes
- FISH probes

Long, single stranded RNAs can be difficult to synthesize and are greatly affected by sequence composition, secondary structure, and applied modifications. Our team routinely synthesizes RNA oligos up to 120 bases. Our scientists work side by side with researchers to determine proper scale, sequence feasibility, and the necessity of purification to provide the greatest percentage of full length RNAs at extended sizes.

It is important to remember that 120 bases is not a limit but a point to which we routinely see success. We are happy to analyze your specific experimental needs to determine likelihood of full length synthesis. Please feel free to contact our Technical Services team to assess your specific requests.




**Analysis of a 105 nucleotide RNA oligo produced with 2' ACE RNA synthesis chemistry.** (A) Analytical ion pairing reversed phase UPLC trace for a 105 nucleotide RNA oligo (with a 5' DMT) showing > 90% full-length material. Oligo was synthesized using 2'-ACE chemistry and purified by HPLC. (B) Mass of the 105 nucleotide RNA oligo was analyzed with the LXQ Mass Spectrometer. Results illustrate the correct mass.

# Illuminate your discoveries

We offer a variety of fluorescent labels for tagging your custom RNAs. Tagging your custom RNAs with fluorescent dyes allows you to visualize localization ensuring proper delivery of your RNA oligo to a desired area of interest.

| Fluorophore | λ max abs (nm) | λ max em (nm) | Color | Comparable to | 5' or 3' |
|---|---|---|---|---|---|
| Fluorescein / 6-FAM | 494 | 520 | | - | both* |
| TAMRA | 565 | 580 | | - | both* |
| Cy3 | 547 | 563 | | - | both* |
| Cy5 | 646 | 662 | | - | both* |
| Cy5.5 | 688 | 707 | | - | both* |

*Some 3' dye labels are only available upon request.

# Chemical modification patterns you can't get anywhere else

We have the siRNA solutions for specificity, stability, or self delivery. Choose one of our specialized chemical modification patterns to enhance your custom siRNA. These proprietary siRNA modifications are available only with Dharmacon pre-designed products or custom siRNA synthesis. Additional modifications available with these proprietary Dharmacon solutions.

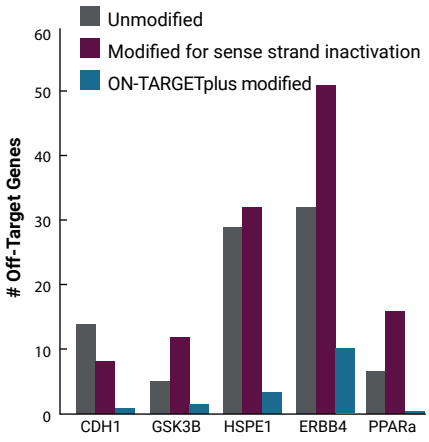
**ON-TARGET™:** Enhanced antisense (guide) strand loading into RISC

**ON-TARGETplus™:** Reduces off-target activity from both strands for premium specificity

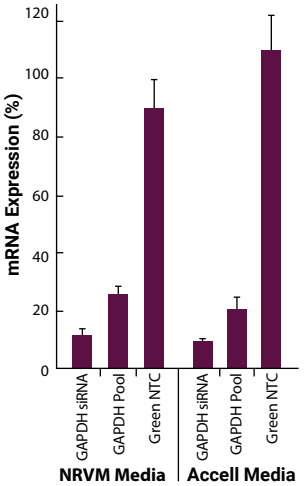
**Accell™:** Delivers siRNA into difficult-to-transfect cells without a transfection reagent

**siSTABLE™:** Greater stability in nuclease-rich environments for *in vivo* applications

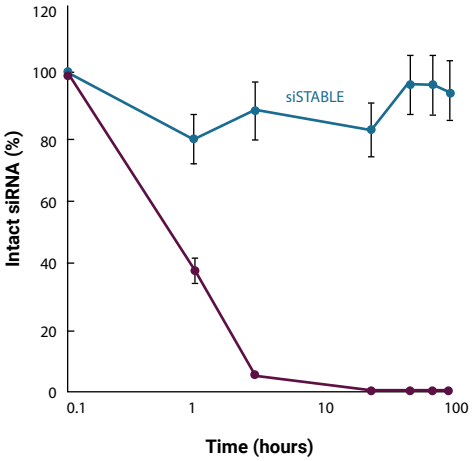
| | ON-TARGET | ON-TARGETplus | Accell | siSTABLE |
|---|---|---|---|---|
| Inhibits sense (passenger) strand uptake by RISC | ★ | ★ | ★ | ★ |
| Antisense strand seed region modified for greater specificity to target | | ★ | | |
| Resistant to endo-and exonuclease degradation | | | ★ | ★ |
| Delivery into cells without transfection reagent | | | ★ | |
| Also available as pre-designed siRNA | | ★ | ★ | |




ON-TARGETplus siRNA dual-strand modification pattern for reduction of off-targets

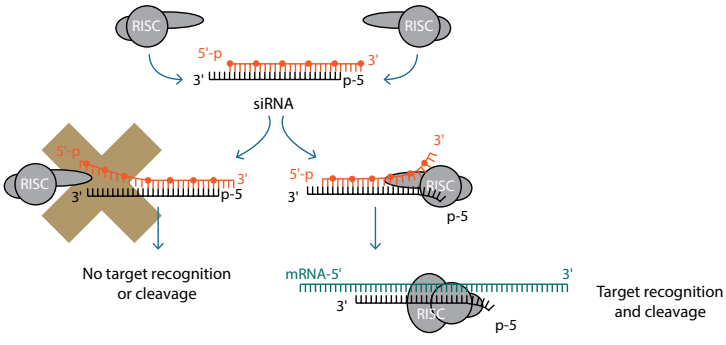



Accell delivery and gene silencing in cardiomyocytes




siSTABLE-modified siRNAs resist degradation by nucleases

ON-TARGET modification ensures antisense strand bias



# What do you value in an RNA provider?

We take pride in our ability to provide you with the highest-quality RNA at a tremendous value. We guarantee to give you the most RNA for your money. Additionally, The Dharmacon 2'-ACE synthesis chemistry and vast chemical modification portfolio provides unsurpassed flexibility and functionality. When value and quality are equally important, trust the RNA experts to meet your needs.

## Long, high yield single strand RNA

Description of RNA processing terms:

**Unprocessed:** The RNA oligo has not undergone any post-synthesis processing; it is not desalted, deprotected, or purified.

**Desalted:** The RNA oligo has been desalted by either ethanol precipitation or C18 column desalting; column desalting is typically employed for PAGE-purified RNA and RNA <10 nt in length.

**Deprotected:** The 2'-ACE protecting groups of the RNA bases have been removed (deprotected).

**PAGE:** The RNA oligo has been purified by polyacrylamide gel electrophoresis.

**HPLC:** The RNA oligo has undergone ion exchange high performance liquid chromatography for purification.

***In vivo:*** The RNA oligo has been processed by counter-ion (Na+) exchange, desalting, sterile filtration, and endotoxin testing.

***In vivo* HPLC:** The RNA oligo has undergone both *in vivo* processing as well as HPLC purification.

| | Un-processed | Desalt/ Deprotect | PAGE* | HPLC* | *In vivo* | *In vivo* HPLC |
|---|---|---|---|---|---|---|
| Deprotected | | ★ | ★ | ★ | ★ | ★ |
| Desalted | | ★ | ★ | ★ | ★ | ★ |
| Endotoxin tested | | | | | ★ | ★ |
| Sodium counter-ion exchange | | | | | ★ | ★ |
| Recommended for 3' or dually labeled RNA | | | ★ | ★ | | ★ |
| Recommended for *in vivo* use | | | | | ★ | ★ |

*** PAGE and HPLC purification options can be requested with or without Desalt/Deprotect**

For more information ↘dharmacon.horizondiscovery.com/custom

**If you have any questions, contact**

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