LNA™ longRNA GapmeR

Potent antisense oligonucleotides for highly efficient inhibition of mRNA and lncRNA function. RNase H-activating LNA™ gapmers designed using advanced algorithms to ensure superior performance and high success rate.

At a glance

- High affinity and high stability LNA™ GapmeRs
- Low toxicity and superior potency
- Less off-target effects and increased ease-of-use with short, single stranded antisense oligonucleotides (ASO)
- High flexibility – target mRNAs and nuclear lncRNAs *in vitro* or *in vivo*
- Save time and effort – sophisticated design algorithms ensure high efficacy

Coverage

LNA™ longRNA GapmeRs can be designed for any RNA target > 80 nucleotides and are available in four different categories depending on application (see also Figure 1):

LNA™ longRNA GapmeR *in vitro* Standard: Cost effective alternative for initial screening of multiple designs using standard cell-lines.

LNA™ longRNA GapmeR *in vitro* Premium. HPLC-purified gapmers with guaranteed purity suitable for most cell assays, also available with 5'or 3' fluorescent labels.

LNA™ longRNA GapmeR *in vivo* Ready. High quality, animal-grade gapmers recommended for any projects that have *in vivo* testing as the ultimate goal. Also recommended for hard-to-transfect cell-lines such as B-cells, T-cells, primary cell lines, cells in suspension etc.

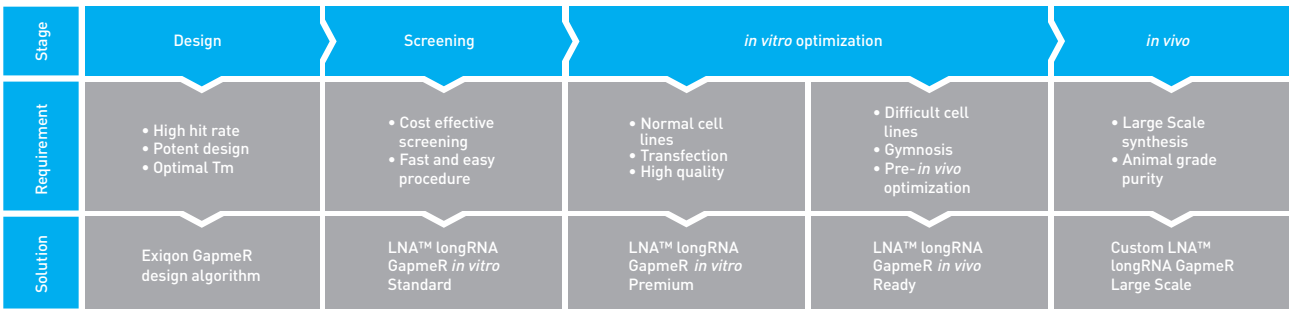
Custom LNA™ longRNA GapmeR – *in vivo* Large Scale. The same high quality and purity as the *in vivo* Ready GapmeRs available with custom large scale yields.

Features

LNA™ longRNA GapmeRs are ASOs used for functional analysis of mRNA and long non-coding RNA, containing a central stretch (gap) of DNA monomers flanked by blocks of LNA™ modified nucleotides (Figure 2). The LNA™ blocks increase the target affinity and nuclease resistance of the oligo and the DNA gap activates RNase H cleavage of the target RNA upon binding. The gapmers are 14-16 nucleotides in length and fully phosphorothioated.

All the LNA™ longRNA GapmeRs are designed using Exiqon's advanced design algorithms to ensure that the ASOs have the optimal combination of length, sequence and LNA™ content, resulting in high-affinity binding and minimal self-annealing. In addition, the algorithms take target sequence accessibility as well as potential non-specific targets into account, leading to high success rates and minimal off-target effects.

Figure 1. Workflow for LNA™ longRNA GapmeRs. Exiqon's gapmers are available for all stages of an inhibition study: from the initial screening to large scale *in vivo* inhibition.



LNA™

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Advantages of LNA™ GapmeRs over siRNA

Antisense technology using LNA™ gapmers offers simple and efficient approaches for the study of gene function and has promising potential in therapeutic applications.

The use of single stranded RNase H-activating ASOs has several advantages over traditional siRNA approaches including fewer off-target effects (due to the lack of a passenger strand), and no issues with saturation of the RISC complex. RNase H-activating ASOs are also able to efficiently target RNAs in the nucleus which make them more suitable for studying the function of nuclear lncRNA.

Besides the conventional methods of delivery, it has been demonstrated recently that LNA™ gapmer ASOs can be taken up in the cell unassisted. The term 'gymnosis' was coined for this process, which denotes naked delivery. Gymnosis can be used to deliver LNA™ gapmers to cell-lines that are difficult to transfect.

LNA™ GapmeRs *in vivo*

Excellent pharmacokinetic and pharmacodynamic properties of LNA™ gapmers have been demonstrated in many different tissues and organs. LNA™ antisense oligonucleotides are well tolerated and show low toxicity *in vivo*. In addition, short, high affinity LNA™ gapmers are active at lower concentrations compared to other antisense oligonucleotides.

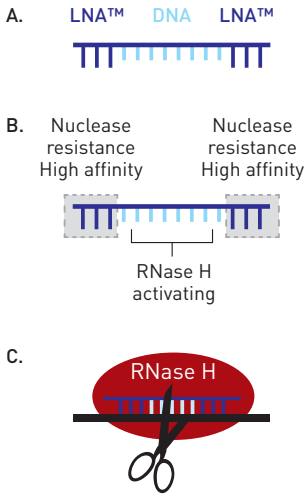
The incorporation of LNA™ increases the serum stability of the ASO. LNA™ gapmer ASOs have also been shown to have high potential in penetrating the cell membrane barrier and successfully interact with the intracellular target site. In addition, formulation (e.g. liposomes or cationic complexes) is not required for efficient delivery *in vivo*, making the workflow easier.

Selected references

- Kole *et al.*, Nature Rev. Drug Disc. 2012
- Zhang *et al.*, Gene Therapy 2011
- Straarup *et al.*, Nucleic Acids Res. 2010
- Stein *et al.*, Nucleic Acids Res. 2010

For more detailed information and publication list, please visit **www.exiqon.com/gapmers**

Figure 2. Structure and function of the LNA™ longRNA GapmeRs. Gapmers contain a DNA part flanked by LNA™ **(A).** The LNA™ parts increase the affinity for the target and confers nuclease resistance **(B).** RNase H is activated by the DNA part of the ASO **(C).**



Ordering information:

Product Description	Product No.
LNA™ longRNA GapmeR, *in vitro* Standard, screening grade, 5 nmol	300600
LNA™ longRNA GapmeR, *in vitro* Premium, cell-culture grade, ready to label, 5 nmol	300601-00
LNA™ longRNA GapmeR, *in vitro* Premium, cell-culture grade, 5' fluorescein label, 5 nmol	300601-04
LNA™ longRNA GapmeR, *in vitro* Premium, cell-culture grade, 3' fluorescein label, 5 nmol	300601-08
LNA™ longRNA GapmeR, *in vivo* Ready, ready to label, 5 nmol or 20 nmol	300602-00 or 300603-00
LNA™ longRNA GapmeR, *in vivo* Ready, 5' fluorescein label, 5 nmol or 20 nmol	300602-04 or 300603-04
LNA™ longRNA GapmeR, *in vivo* Ready, 3' fluorescein label, 5 nmol or 20 nmol	300602-08 or 300603-08
Custom LNA™ longRNA GapmeR, for *in vivo* use, modifications on demand, custom large scale (mg)	500175

Contact information

Outside North America
Phone: +45 45 65 09 29 · Fax: +45 45 66 18 88
North America
Phone: +1 781 376 4150 · Fax: +1 781 376 4152

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