



# NittoPhase<sup>®</sup>HL Solid Support

## High Loaded Polymeric Solid Supports for Oligonucleotide Synthesis

A Revolutionary Solid Support with Loading as high as 400  $\mu\text{mol/g}$  for DNA and 250  $\mu\text{mol/g}$  for RNA Synthesis

- **Maximal Loading Capacity**—Robust design enables maximum loading capacity on the market, delivering synthesis yields at unprecedented levels.
- **Reduced Oligonucleotide Synthesis Costs**—High loading allows greater synthesis scale per column volume, resulting in outstanding per micromole synthesis cost savings.
- **Proven Performance in Large Scale Therapeutic Oligonucleotide Synthesis**—NittoPhase<sup>®</sup>HL has shown excellent results in small to large scale GMP (up to 900 mmole) synthesis of therapeutic oligonucleotides.
- **Superior Flexibility**—NittoPhase<sup>®</sup>HL has been widely applied for syntheses of RNA, longmers and modified oligonucleotides at higher loadings than ever before.
- **Outstanding Quality**—NittoPhase<sup>®</sup>HL is manufactured and loaded in compliance with ISO9001:2008 quality management system standards.
- **Diversified Product Offering**— NittoPhase<sup>®</sup>HL solid supports are available in a variety of loading levels with all standard deoxy and ribo bases, Universal Linker, and a wide range of modified custom linkers.

Since its launch in 2004, NittoPhase<sup>®</sup> has become the leading solid support in the therapeutic oligonucleotide synthesis market, with a strong track record of proven performance in large scale GMP synthesis.

Kinovate has redefined the boundaries of solid phase oligonucleotide synthesis with the introduction of NittoPhase<sup>®</sup>HL High Loading Support, which has superb results at scales as high as 900 mmol.

Improved yields and purities, together with the elevated loading capacities, undoubtedly empower NittoPhase<sup>®</sup>HL to offer superior performance at lower unit cost for oligonucleotide synthesis.

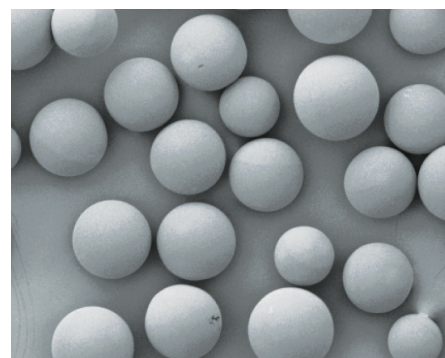


Figure 1. SEM image of NittoPhase<sup>®</sup>HL Solid Support.

Table 1. NittoPhase<sup>®</sup>HL Solid Support properties.

Properties	Characteristics
Polymer Matrix	Cross-linked polystyrene
Functionality	Hydroxyl group
# of Hydroxyl Group	550 $\mu\text{mol/g}$
Average Particle Size	85 $\mu\text{m}$
Average Pore Size	45 nm
Dry Volume	2.7 ml/g
Optimal Loading Capacity	200-400 $\mu\text{mol/g}$
Swelling Volume (in acetonitrile)	4.0 ml/g
Swelling Volume (in toluene)	6.1 ml/g
Leaching	None

# Superior Performance from Lab to Commercial Scale

## i) Lab Scale

Table 2. Results of lab scale DNA & RNA oligo synthesis with NittoPhase®HL Solid Support.

NittoPhase®HL Loading	Sequence	Synthesis Scale (μmol)	Crude Yield (OD <sub>260</sub> /μmol)	Purity (%)
T200	RNA 21mer	165	106	79
T250*	RNA 21mer	176	99	84
T350	DNA 20mer	283	128	83
T400	DNA 20mer	307	135	83
UnyLinker™350	DNA 20mer	290	134	83

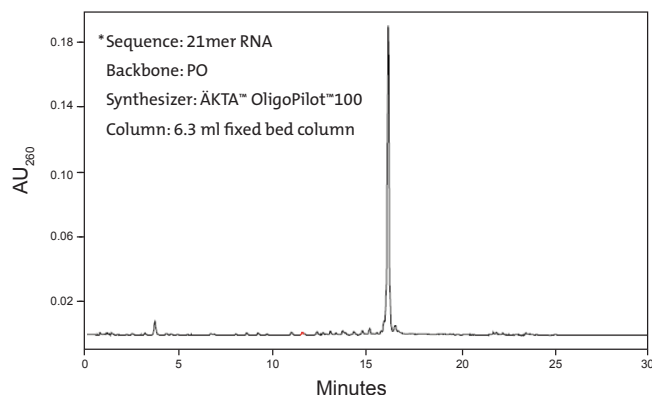


Figure 2. IP-HPLC Trace for NittoPhase®HL T250 RNA synthesis.

## ii) Medium Scale

Table 3. Results of mid-scale DNA & highly modified RNA oligo synthesis with NittoPhase®HL Solid Support.

NittoPhase®HL Loading	Sequence	Synthesis Scale (mmol)	Crude Yield (OD <sub>260</sub> /μmol)	Purity (%)
Modified250**	RNA 21mer	2	S 145	79
			AS 142	84
UnyLinker™330*‡	DNA 16mer	2	105	83
UnyLinker™350‡	DNA 20mer	2	101	80
UnyLinker™400‡	DNA 20mer	2	94	73

\*\* In collaboration with Quark Pharmaceuticals, Inc.

‡ Data Courtesy of Isis Pharmaceuticals, Inc.

S = Sense strand, AS = Antisense strand

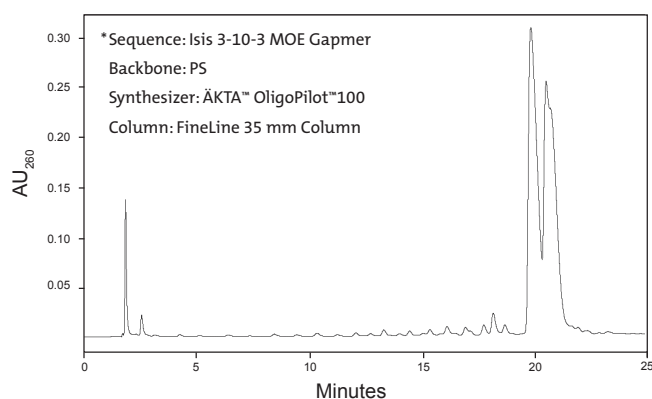


Figure 3. IP-HPLC Trace for NittoPhase®HL UnyLinker™330 DNA synthesis.

## iii) Clinical Scale

Table 4. Results of clinical-scale DNA & highly modified RNA oligo synthesis with NittoPhase®HL Solid Support.

NittoPhase®HL Loading	Sequence	Synthesis Scale (mmol)	Crude Yield (OD <sub>260</sub> /μmol)	Purity (%)
Modified250***	RNA 21mer	65	S 151	76
			AS 136	79
UnyLinker™315‡	DNA 20mer	550	111	86
UnyLinker™315‡	DNA 20mer	700	112	90
UnyLinker™315**	DNA 20mer	900	105	83

\*\*\* In collaboration with NITTO DENKO Avecia Inc. & Quark Pharmaceuticals, Inc.

‡ Data Courtesy of Isis Pharmaceuticals, Inc.

S = Sense strand, AS = Antisense strand

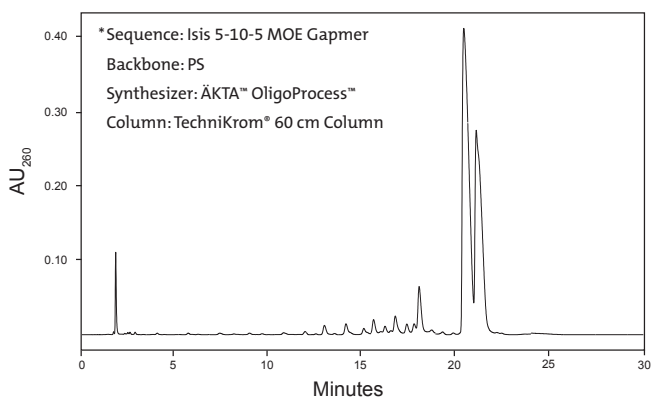


Figure 4. IP-HPLC Trace for NittoPhase®HL UnyLinker™ DNA synthesis.

For more information, please visit [www.kinovate.com](http://www.kinovate.com) or contact [info@kinovate.com](mailto:info@kinovate.com)

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