KINOVATE LIFE SCIENCES

NittoPhase®HL Solid Support

High Loaded Polymeric Solid Supports for Oligonucleotide Synthesis

A Revolutionary Solid Support with Loading as high as 400 µmol/g for DNA and 250 µmol/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®HL has shown excellent results in small to large scale GMP (up to 900 mmole) synthesis of therapeutic oligonucleotides.
- **Superior Flexibility**—NittoPhase®HL has been widely applied for syntheses of RNA, longmers and modified oligonucleotides at higher loadings than ever before.
- **Outstanding Quality**—NittoPhase®HL is manufactured and loaded in compliance with ISO9001:2008 quality managment system standards.
- **Diversified Product Offering**— NittoPhase®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.

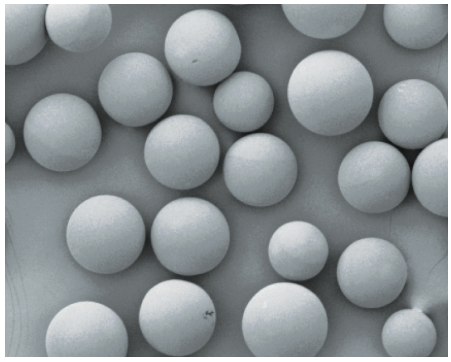

Figure 1. SEM image of NittoPhase®HL Solid Support.

Table 1. NittoPhase®HL Solid Support properties.

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

Since its launch in 2004, NittoPhase® 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®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®HL to offer superior performance at lower unit cost for oligonucleotide synthesis.

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_{260}/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

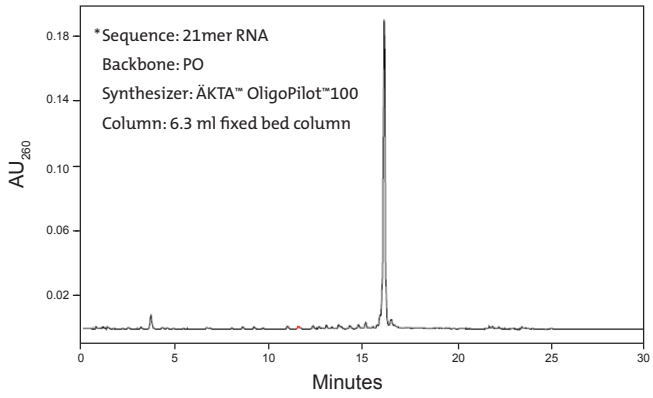

Figure 2. IP-HPLC Trace for NittoPhase®HL T250 RNA synthesis.

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_{260}/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

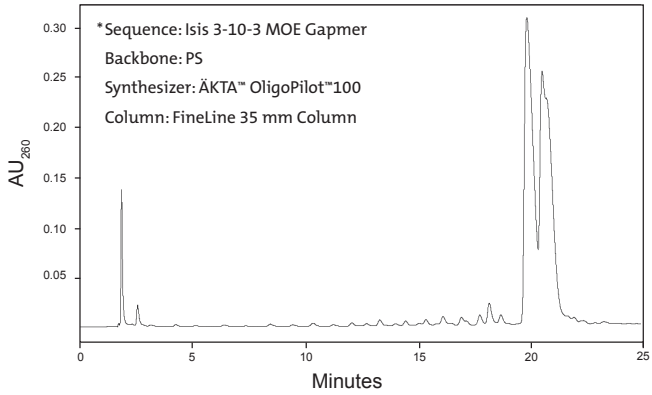

Figure 3. IP-HPLC Trace for NittoPhase®HL UnyLinker™330 DNA synthesis.

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_{260}/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

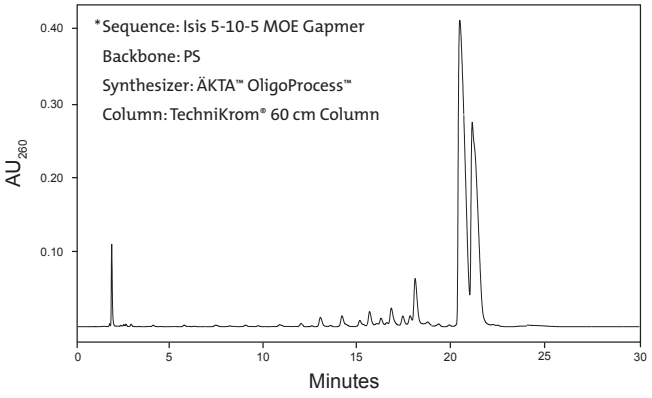

Figure 4. IP-HPLC Trace for NittoPhase®HL UnyLinker™ DNA synthesis.

For more information, please visit www.kinovate.com or contact info@kinovate.com

COMPANY WITH QUALITY SYSTEM CERTIFIED BY DNV = ISO 9001:2008 =

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