# Nitto Denko Corporation and Isis Pharmaceuticals, Inc. Announce Introduction of a High Performance Synthesis Product for the Manufacture of Oligonucleotides

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- New Solid Support Should Significantly Decrease Cost of Goods -

OSAKA, Japan, OCEANSIDE, Calif. and CARLSBAD, Calif., Nov. 9 /PRNewswire-FirstCall/ -- Nitto Denko Corporation, a leading multi-national polymer company, and Isis Pharmaceuticals, Inc. (Nasdaq: ISIS), a leader in RNA-based drug discovery and development, announced today that they have jointly developed a new high performance solid support for the manufacture of oligonucleotides.

Solid support is the base structure used in the synthesis of oligonucleotides, both antisense, including RNA and DNA-based and RNAi, and aptamer drugs and represents a substantial portion of the cost to manufacture these drugs. The new solid support has the potential to decrease manufacturing costs in two ways: First, it is less expensive than currently used solid supports. Second, it has the potential to increase yield, thereby further reducing cost-of-goods.

Nitto Denko Corporation and Nitto Denko Technical Corporation, a dedicated research and development facility located in Oceanside, CA, designed and engineered the core technology for the future solid support. In collaboration with Isis Pharmaceuticals, the technology was then tested and optimized for oligonucleotide synthesis. The product will be marketed by Kinovate Life Sciences, Inc., also a wholly owned subsidiary of Nitto Denko Corp., located in Oceanside. Isis will receive royalties on sales of this innovative new solid support.

"As an innovator in RNA-based drug discovery and development, Isis is also a leader in the development of manufacturing standards for oligonucleotides. This new solid support product enhances our ability to efficiently develop drugs that improve the lives of patients. Further, it is an important component in our strategy to encourage and facilitate the biotechnology industry's interest in RNA-based technologies through partnering with outstanding companies like Nitto Denko," said B. Lynne Parshall, Executive Vice President and Chief Financial Officer of Isis.

Nitto Denko Technical Corporation's President, Dr. Kenji Matsumoto commented that: "Through Isis' expertise in oligonucleotides and our leadership in polymer chemistries, our companies have made a significant step forward in the field of oligonucleotide synthesis," adding that "This material has been demonstrated to have superior performance across all criteria in both small and large scale synthesis. We are extremely pleased and fortunate to have been involved with Isis, the leader in the field of RNA-based therapeutics. Such collaboration underscores NDT and Kinovate's emerging position as leaders in the field of life sciences."

ABOUT SOLID SUPPORT

Manufacture of oligonucleotide drugs involves use of solid support matrix upon which chemical reactions happen in a cyclic manner. The reactions are performed in a synthesizer and are fully automated. At the end of synthesis, drugs are purified by high performance liquid chromatography and characterized extensively to check their authenticity and purity. Thus solid support plays a crucial role in the manufacture of oligonucleotide drugs. It is increasingly believed that the yield of an oligonucleotide synthesis is greatly influenced by the proper design of a polymeric support which undergoes roughly eighty chemical reactions in about eight hours for a 20-mer oligonucleotide.

ABOUT ISIS PHARMACEUTICALS, INC.

Isis Pharmaceuticals, Inc. is exploiting its expertise in RNA to discover and develop novel human therapeutic drugs for its pipeline and for its partners. The company has successfully commercialized the world's first antisense drug and has 12 antisense products in development to treat metabolic, cardiovascular, inflammatory and viral diseases, and cancer. Through its Ibis Therapeutics® program, Isis is developing a biosensor to identify infectious organisms, and discovering small molecule drugs that bind to RNA. As an innovator in RNA-based drug discovery and development, Isis is the owner or exclusive licensee of more than 1,400 issued patents worldwide. Additional information about Isis is available at www.isispharm.com.

ABOUT NITTO DENKO CORPORATION

Incorporated in 1918 and having its head office in Osaka, Japan, Nitto Denko Corporation designs, manufactures and sells a wide

range of products including adhesive tapes, electronic components, and medical equipments, based on its core technologies of high polymer synthesis. The company holds approximately 60% share of the global market for polarizing films. Polarizing film is a core material used in liquid crystal display television production. Nitto Denko's applied products are widely used in medical instruments, automobiles and electronics, accounting for 70% of its total sales. The company remains focused on attaining "Global Niche Top" status in many of its core products. The company has 10 divisions and consolidated group sales in fiscal year 2004 amounted to US$4.2 billion. Additional information about Nitto Denko Corporation is available at www.nitto.com.

ABOUT NITTO DENKO TECHNICAL CORPORATION

Nitto Denko Technical Corporation is a dedicated research and development facility established in October 2000 at Oceanside, California, USA. As a subsidiary of Nitto Denko Corporation, it is involved in research of sophisticated technologies in a variety of new advanced scientific areas, such as novel materials and devices spanning from optical communication to genetic engineering.

Nitto Denko Technical Corporation (NDT) has two R&D divisions-biomedical and optical communication areas. The biomedical division has extensively studied novel gene-delivery technology, tissue engineering, and bio-diagnosis technology. The optical communication division focuses and develops new polymer-based photorefractive materials. In order to accommodate the rapidly growing divisions, a new and independent research facility for NDT is in plans to be opened at the beginning of 2005. More information about NDT can be found at www.ndtcorp.com.

ABOUT KINOVATE LIFE SCIENCES

Kinovate Life Sciences is a new venture capital company, fully seed funded by Nitto Denko Corporation. Kinovate's mission of commercialization and marketing of life science-related technologies developed at NDT place it at the cutting edge of gene-delivery technology. Kinovate's first product, CytoPure, a biodegradable polymer transfection reagent was launched soon after the company's inception in January of this year. Subsequent gene-delivery related products are expected to be launched in late 2004-early 2005. The solid support for oligonucleotide synthesis developed with Isis Pharmaceuticals is expected to provide a significant stimulus to the Kinovate business.

ISIS FORWARD-LOOKING STATEMENT

This press release contains forward-looking statements concerning discovery, development and therapeutic potential of RNA-based technology and drugs, the potential success of Isis' collaboration with Nitto Denko and the potential of the company's intellectual property position. Any statement describing our goals, expectations, intentions or beliefs is a forward-looking statement and should be considered an at-risk statement, including those statements that are described as Isis' clinical goals. Such statements are subject to certain risks and uncertainties, particularly those inherent in the process of developing technology and systems used to identify infectious agents, in discovering and commercializing drugs that are safe and effective for use as human therapeutics and in the endeavor of building a business around such products and services. Actual results could differ materially from those discussed in this press release. As a result, you are cautioned not to rely on these forward-looking statements. These and other risks concerning Isis' research and development programs are described in additional detail in Isis' Annual Report on Form 10-K for the year ended December 31, 2003, and quarterly report on Form 10-Q for the quarter ended September 30, 2004, which are on file with the U.S. Securities and Exchange Commission. Copies of these and other documents are available from the company.

NITTO DENKO FORWARD-LOOKING STATEMENT

This press release contains forward looking statements concerning research & development of polymer materials related to the life sciences area developed by Nitto Denko Corporation and its subsidiaries, including solid support for oligonucleotide synthesis. Any and all statements concerning Nitto's claims, intentions, beliefs, etc. should be considered forward looking statements and as such at-risk. Statements made above, including those concerning testing results should be considered observed values, not guaranteed values, and actual results may differ materially from those mentioned above. Readers of this press release are cautioned to not rely solely on the forward-looking statements contained above.

Nitto Denko Technical Corporation and Kinovate Life Sciences, Inc. are wholly owned subsidiaries of Nitto Denko Corporation.

SOURCE Isis Pharmaceuticals, Inc.
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