NEKTAR THERAPEUTICS
Form 10-K/A
May 09, 2005
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UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, DC 20549

FORM 10-K/A

Amendment No. 1

FOR ANNUAL AND TRANSITION REPORTS PURSUANT TO SECTIONS 13 OR 15(d)

OF THE SECURITIES EXCHANGE ACT OF 1934

¨ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934.**
For the fiscal year ended December 31, 2004

or,

¨ **TRANSITION REPORTS PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934.**
Commission File Number: 0-23556

NEKTAR THERAPEUTICS

(Exact name of registrant as specified in its charter)

Delaware	**94-3134940**
(State or other jurisdiction of incorporation or organization)	**(IRS Employer Identification No.)**

150 Industrial Road

San Carlos, California 94070

(Address of principal executive offices and zip code)

650-631-3100

(Registrant s telephone number, including area code)

Securities registered pursuant to Section 12(b) of the Act: **None**

Securities registered pursuant to Section 12(g) of the Act: **Common Stock, $0.0001 par value**

Indicate by check mark whether the Registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the Registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ¨ No ¨

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of Registrant s knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ¨

Indicate by check mark whether the registrant is an accelerated filer (as defined in Exchange Act Rule 12b-2). Yes ¨ No ¨

The approximate aggregate market value of voting stock held by non-affiliates of the Registrant, based upon the last sale price of the Registrant s Common Stock on June 30, 2004 as reported on the NASDAQ National Market was approximately $1,655,474,516. This calculation excludes approximately 798,878 shares held by directors and executive officers of the Registrant. Exclusion of these shares should not be construed to indicate that such person controls, is controlled by or is under common control with the Registrant. This calculation does not exclude shares held by organizations whose ownership exceeds 5% of the Registrant s outstanding Common Stock as of June 30, 2004 that have represented to the Registrant that they are registered investment advisers or investment companies registered under Section 8 of the Investment Company Act of 1940. Determination of affiliate status for the purposes of this calculation is not necessarily a conclusive determination for any other purpose.

84,730,751

(Number of shares of common stock outstanding as of February 28, 2005)

DOCUMENTS INCORPORATED BY REFERENCE

Portions of Registrant s definitive Proxy Statement to be filed for its 2005 Annual Meeting of Stockholders are incorporated by reference into Part III hereof.

EXPLANATORY NOTE

We are filing this amendment to our Annual Report on Form 10-K, originally filed with the Securities and Exchange Commission on March 14, 2005, for the purpose of: (1) amending Item 6; (2) amending Item 7; (3) amending Item 8, and (4) amending Item 14. The filing of this Form 10-K/A Amendment No.1 reflects (1) reclassification of certain auction rate securities from cash equivalents to short-term investments as of December 31, 2004 and 2003, and (2) enhanced disclosure of securities pledged as collateral for certain letters of credit that were outstanding as of December 31, 2004 and 2003. Except as indicated above, no other information included in the Annual Report on Form 10-K is amended by this Form 10-K/A Amendment No. 1. While we are amending only certain portions of our Form 10-K, for convenience and ease of reference, we are filing the entire Form 10-K, except for certain exhibits. Accordingly, this Form 10-K/A should be read in conjunction with our originally filed Form 10-K filed on March 14, 2005 with the Securities and Exchange Commission.

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NEKTAR THERAPEUTICS

2004 ANNUAL REPORT ON FORM 10-K/A, AMENDMENT NO. 1

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Forward-Looking Statements

This report includes forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended (the 1933 Act) and Section 21E of the Securities Exchange Act of 1934, as amended (the 1934 Act). All statements other than statements of historical fact are forward-looking statements for purposes of this annual report, including any projections of earnings, revenues or other financial items, any statements of the plans and objectives of management for future operations, any statements concerning proposed new products or services, any statements regarding future economic conditions or performance and any statement of assumptions underlying any of the foregoing. In some cases, forward-looking statements can be identified by the use of terminology such as may, will, expects, plans, anticipates, estimates, p or continue, or the negative thereof or other comparable terminology. Although we believe that the expectations reflected in the forward-looking statements contained herein are reasonable, there can be no assurance that such expectations or any of the forward-looking statements will prove to be correct and actual results could differ materially from those projected or assumed in the forward-looking statements. Our future financial condition and results of operations, as well as any forward-looking statements, are subject to inherent risks and uncertainties, including but not limited to the risk factors set forth below and for the reasons described elsewhere in this annual report. All forward-looking statements and reasons why results may differ included in this report are made as of the date hereof and we do not intend to update any forward-looking statements except as required by law or applicable regulations.

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PART I

Item 1. Business

General

Our business focuses on creating high value products through the application of advanced drug delivery technologies. We have three drug delivery platforms that are designed to improve the performance of molecules. These platforms are: Nektar Advanced PEGylation Technology, Nektar Pulmonary Technology, and Nektar Supercritical Fluid (SCF) Technology.

Our mission is to develop superior therapeutics to make a difference in patients lives. We pursue our mission in two ways. First, we partner with pharmaceutical and biotechnology companies that seek to improve and differentiate their products. In addition, we are in the early-stages of development of our own proprietary products. We are working to become one of the world s leading drug delivery products companies.

Our product pipeline includes both partnered and proprietary products. We have ongoing collaborations with more than 20 biotechnology and pharmaceutical companies to provide our drug delivery technologies. Our partner product pipeline includes: six products (Neulasta®, PEGASYS®, Somavert®, PEG-INTRON®, Definity®, and Macugen®) approved by the U.S. Food and Drug Administration (FDA); one additional product (SprayGel) approved in Europe that is in late stage testing in the U.S., one product (Exubera®) for which a New Drug Application (NDA) has been filed with the FDA, two products (Exubera® and Macugen®) for which a marketing authorization application has been filed with the European Medicines Evaluation Agency (EMEA); two additional products (CDP 870 and CERA) in Phase III or pivotal trials; and ten products in Phase I and Phase II trials. In addition to our partnered product programs, we have four proprietary products in the early stages of development. One of these products involves an inhaled small molecule that has entered a Phase I trial and another product is in proof-of-concept human studies. The remaining two products are in preclinical testing.

We intend to continue to identify and capitalize on technologies and markets where we see opportunities to establish leadership positions.

Strategy

The key elements of our business strategy are to:

Partner with Pharmaceutical and Biotechnology Companies. We have collaborations with more than 20 pharmaceutical and biotechnology companies. We believe our partnering strategy enables us to develop a large and diversified pipeline of drug products that use our technologies.

In a typical Nektar Pulmonary Technology collaboration, our partner will provide the active pharmaceutical ingredient (the majority of which are already approved by the FDA in another delivery form), fund development, obtain regulatory approvals, and market the

resulting commercial product. We supply our technology and we may manufacture and supply the device and/or drug formulation. In consideration for our efforts, we typically receive R&D reimbursement, milestone payments, revenues from clinical drug manufacturing, as well as royalties from commercial sales of products. In addition, for products using our Pulmonary Technology, we typically receive revenues from the supply of our device for the product along with revenues for drug processing or filling once the product is commercially available.

In a typical Nektar Advanced PEGylation Technology collaboration, we manufacture and supply the polyethylene glycol (PEG) reagents to our partners and we may receive milestone payments, manufacturing revenues and in some cases, royalties from sales of the PEGylated commercial product.

Develop Our Own Proprietary Products Utilizing Nektar Technology and/or Know-how. We typically use our know-how and technology in combination with approved drugs to develop our own proprietary products. We focus on identifying off-patent or near off-patent compounds that would benefit from the application of our

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technologies to improve the performance and/or delivery of these compounds. Our objective is to create value by advancing these molecules into clinical development and then determining the most appropriate stage to partner these based on the cost and complexity of development and the needs for commercialization. For those molecules that have complex and costly development paths and/or require significant commercial support, we may choose to seek a commercialization partner at an earlier stage. We plan to make partnering decisions for our proprietary products on a product by product basis taking into consideration both market as well as internal factors.

Overview of Nektar Technologies

Our drug delivery technology platforms are designed to improve the performance of both new and existing chemical entities whether they are small molecules or macromolecules. Improved performance typically includes one or more of the following attributes: improved efficacy, improved safety, improved convenience, or enabling the development of a drug molecule. Our three technology platforms are:

Nektar Advanced PEGylation Technology uses advanced PEGylation chemistry and a PEG-based delivery system to enhance the performance of most major drug classes, including macromolecules such as peptides and proteins, smaller sized molecular compounds and other drugs. Nektar Advanced PEGylation Technology is used in six products approved for use in the U.S. and in one additional product approved in Europe.

Nektar Pulmonary Technology uses our know-how and technology in drug formulation, powder processing, powder filling and packaging and devices to create an integrated system to reproducibly deliver therapeutics to the lung for both systemic and local lung applications. The most advanced product using this technology is Exubera® (inhaled insulin), which is under development by Pfizer Inc. (Pfizer) and The Sanofi-Aventis Group (Sanofi-Aventis) and for which a marketing authorization application has been filed with the EMEA and an NDA has been filed with the FDA in the U.S.

Nektar Supercritical Fluid (SCF) Technology uses a novel particle engineering process that yields consistent powder particles in terms of size, shape and morphology that can be incorporated into a number of dosage forms including tablets, capsules, and inhalation systems. We are in the process of scaling-up our SCF Technology to support later stage development and eventually provide commercial manufacturing. We believe our SCF Technology may serve as a platform technology for a diverse range of applications primarily for small molecules including such uses as taste masking and selection of stable solid state forms that can affect both the rate and extent of absorption of certain drugs.

NEKTAR ADVANCED PEGYLATION TECHNOLOGY

Nektar Advanced PEGylation Technology is designed to enhance performance of most drug classes including macromolecules, such as peptides and proteins, as well as small molecules and other drugs. PEGylation is a chemical process where PEG chains are attached to active therapeutic molecules. The advantages of Nektar Advanced PEGylation Technology include the potential to: improve drug solubility and stability; increase drug half-life; reduce immune responses to an active drug; and improve the efficacy and/or safety of a molecule in certain instances.

We use our Advanced PEGylation Technology in both our partnered and proprietary programs. In a typical partner collaboration, we derive revenue from milestone payments during research and development and may receive royalties on sales of approved products or other PEG applications. We may also receive additional revenue from manufacturing the PEG reagent used by our partners.

Nektar Advanced PEGylation Technology is used in six products approved for use in the U.S. and in one additional product approved in Europe.

Characteristics of Nektar Advanced PEGylation Technology. PEG is a neutral, water soluble, non-toxic polymer and is one of the few synthetic polymers approved for internal use by the FDA in a variety of foods, cosmetics, personal care products and pharmaceuticals.

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We believe our Advanced PEGylation Technology can offer one or more of the following benefits:

Prolonged duration of action thereby reducing the need for frequent injections by both reducing the rate of absorption from a subcutaneous injection and reducing the rate of elimination or metabolism.

Reduced immune response to certain macromolecules which may prolong their effectiveness with repeated doses if the antibodies are neutralizing.

Improved stability which not only contributes to the prolonged duration of activity but may facilitate the formulation of a stable liquid formulation where previously the product had to be lyophilized.

Improved efficacy and/or safety in certain instances. Although PEGylation often reduces the potency of a drug, this loss in activity can be more than offset by an improvement in the pharmacokinetics especially for drugs in which a prolonged residence time in the body translates to improved efficacy.

Applications of Nektar Advanced PEGylation Technology. We believe our Advanced PEGylation Technology can be useful in many applications, including the following:

***PEG for Pharmaceutical Use*.** PEGs can be attached to different types of molecules including proteins, peptides, antibodies and oligonucleotides and may substantially enhance their therapeutic value.

PEG for Medical Device Use. PEGs can be used in various medical device applications including their use in the formulation of gels that can act as post-surgical seals or to prevent post-surgical adhesions. Nektar PEG is currently being used by Confluent Surgical Inc. for these applications.

PEG-Liposomes. The incorporation of PEG onto the outer coating of a type of lipid membrane (liposomes), increases the lifetime of a serum which can provide controlled and specific delivery of certain drugs.

NEKTAR PULMONARY TECHNOLOGY

Nektar Pulmonary Technology is designed to enable efficient and reproducible deep lung delivery of a variety of molecule types across a wide range of doses. Specifically, our development of spray-dried formulations of drug particles potentially enables efficient dispersion and reproducible delivery of both large and small molecules deep within the lung for systemic and local lung indications.

Nektar Pulmonary Technology integrates several unique technologies including customized formulation of drug compounds, dry powder processing, filling and packaging along with proprietary inhalation devices to enable efficient and consistent delivery of both macromolecule and small molecule drugs to the deep lung. For specific drug products, we typically formulate and process bulk active pharmaceutical ingredients supplied by collaborative partners into dry powders, which are packaged into individual dosing units based upon product requirements.

Dry Powder Formulations for Pulmonary Delivery. Each drug poses different formulation challenges due to differing chemical and physical characteristics and dosing requirements. As a result, optimization is required for each specific drug. We apply our know-how and technology to achieve intrinsically dispersible powders and integrate them into pulmonary delivery devices in order to provide an easy-to-use and reproducible delivery system across a wide range of conditions and patient use scenarios. In the area of macromolecules, we have developed several protein powders, which remain stable at room temperature in excess of one year. Through our work with numerous macromolecules, we are developing an extensive body of knowledge on aerosol dry powder formulations. We have filed and expect to continue to file patent applications on several of our formulations and, through acquisitions of intellectual property, have acquired rights to certain U.S. and foreign patents and patent applications relating to stabilization of macromolecule drugs in dry powder formulations.

Powder Processing. We modify standard powder processing equipment and develop custom techniques to produce fine dry powders with particle diameters typically between one and five microns. We have scaled up

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powder processing to levels sufficient for producing candidate powders for late stage clinical trials. We expect that production at these levels will be sufficient to satisfy the needs of small volume commercial products. We are also in the process of further scaling up our powder processing systems in order to produce quantities sufficient for commercial production of products we believe we will need to supply in high volumes, such as Exubera®.

Powder Filling and Packaging. Powders made up of fine particles intended for inhalation typically require handling that is technically more challenging than for powders comprised of larger particles. We have developed and are internally qualifying a proprietary automated filling system suitable for use in production of clinical trial supplies and, for certain products, in production of commercial quantities. The underlying technology is intended to allow its application to a broad variety of powder types, characteristics, and a wide range of target fill masses.

Nektar Proprietary Pulmonary Inhalers. We have developed a range of devices to appropriately address most pulmonary product needs. These devices will deliver aerosols over a wide range of doses and use scenarios. We have a durable device that is targeted towards the chronic use scenario, such as Exubera® (inhaled insulin). We also have a semi-durable device that can be used for shorter durations of therapy as well as chronic use applications. In addition, certain of our powders appear to be well suited for use in metered dose inhalers. Depending on the market needs for any given product, we will select a device that best meets those needs.

To date, there are no products using our Pulmonary Technology that have been approved for use and there can be no assurance that our pulmonary technology will be approved for use or will be a successful or commercially viable technology or will work for any of its intended uses.

NEKTAR SUPERCRITICAL FLUID TECHNOLOGY

Our SCF Technology uses supercritical carbon dioxide to disperse and mix a stream of drug solution while simultaneously extracting the organic solvent resulting in a rapid formation of a drug or drug/excipient particle. This is achieved by metering the solution and the supercritical fluid into a particle formation vessel held under controlled conditions of temperature and pressure above the critical point of the supercritical fluid-solvent mixture. Particles are then recovered from the particle formation vessel. SCF Technology may offer an alternative to typical crystallization processes for many small molecules with the potential benefits of better control over particle size, form, structure, and surface characteristics.

We believe our SCF Technology may serve as a platform technology for a diverse range of applications primarily for small molecules including such uses as taste masking and selection of stable solid state forms that can affect both the rate and extent of absorption of certain drugs.

Currently, there are no approved products that use our SCF technology. There can be no assurance that our SCF Technology will be approved for use or will be a successful or commercially viable technology.

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CLINICAL PIPELINE

The following table summarizes our partnered pipeline including those in clinical development, those filed for registration and those approved. The table includes the primary indication for the product, the identity of a respective corporate partner if one has been disclosed, and the status of the program. Approval status applies to the U.S. market unless otherwise noted.

Molecule	Primary Indication	Partner	Status(1)
Neulasta® (pegfilgrastim)	Neutropenia	Amgen Inc.	Approved
PEGASYS® (peginterferon alfa-2a)	Hepatitis-C	Hoffmann-La Roche Ltd.	Approved
Somavert® (pegvisomant)	Acromegaly	Pfizer Inc.	Approved
PEG-INTRON® (peginterferon alfa-2b)	Hepatitis-C	Schering-Plough Corporation	Approved
Definity® (PEG)	Cardiac imaging	Bristol-Myers Squibb Company	Approved
Macugen® (pegaptanib sodium injection)	Age-related macular degeneration	Eyetech Pharmaceuticals, Inc	Approved in the U.S. & Filed in the EU & Canada
Macugen® (pegaptanib sodium injection)	Diabetic macular edema	Eyetech Pharmaceuticals Inc.	Phase II
Exubera® (inhaled insulin)	Diabetes	Pfizer Inc.	Filed in the U.S. and Europe
SprayGel adhesion barrier system (PEG-hydrogel)	Prevention of post-surgical adhesions	Confluent Surgical Inc.	Pivotal trials in U.S. Approved in Europe
CDP 870 (PEG-anti-TNF alpha antibody fragment)	Rheumatoid arthritis	UCB Pharma	Phase III
	Crohn s disease		Phase III
CERA (Continuous Erythropoiesis Receptor Activator)	Renal anemia	Hoffmann-La Roche Ltd.	Phase III
Undisclosed (PEG)	Undisclosed	Undisclosed	Phase II
CDP 791 (PEG-antibody fragment angiogenesis inhibitor)	Cancer	UCB Pharma	Phase I/II
CDP 484 (PEGylated antibody fragment targeting pro-inflammatory cytokine interleukin 1-beta)	Rheumatoid Arthritis	UCB Pharma	Phase I/II
Tobramycin inhaled powder (TIP)	Lung infection	Chiron Corporation	Phase I
Inhaled leuprolide	Endometriosis	Enzon Inc.	Phase I
MARINOL® (inhaled dronabinol)	Multiple indications	Solvay Pharmaceuticals, Inc.	Phase I
PEGylated interferon beta	Undisclosed	Serono, Inc.	Phase I
PEG-Alfacon (PEGylated interferon alfacon-1)	Hepatitis-C	InterMune, Inc.	Phase I
PEGylated-AXOKINE	Obesity	Regeneron Pharmaceuticals	Phase I
Undisclosed (PEG)	Undisclosed	Pfizer Inc.	Phase I

(1) Status definitions are as follows:
Approved regulatory approval to market and sell product obtained in the U.S. or EU.

Phase III or Pivotal Product in large-scale clinical trials conducted to obtain regulatory approval to market and sell a drug. Typically, these trials are initiated following encouraging Phase II trial results.

Phase II Product in clinical trials to establish dosing and efficacy in patients.

Phase I Product in clinical trials typically in healthy subjects to test safety.

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NEKTAR PARTNER DEVELOPMENT PROGRAMS

FDA Approved Products

Neulasta® (pegfilgrastim)

We entered into a license, manufacturing and supply agreement with Amgen Inc. in July 1995 whereby we licensed to Amgen one of our PEG reagents used in the manufacture of Amgen s Neulasta® product. Neulasta® was approved by the FDA in 2002 for use in reducing the incidence of infection as manifested by febrile neutropenia, in patients with nonmyeloid malignancies receiving myelosuppressive anticancer drugs. Approval for use in similar indications for Neulasta® was granted in Europe and Australia the same year.

PEGASYS® (peginterferon alfa-2a)

We entered into a license, manufacturing and supply agreement with F. Hoffmann-La Roche Ltd. (Roche) in February 1997, whereby we licensed to Roche one of our PEG reagents used in the manufacture of Roche s PEGASYS® (peginterferon alfa-2a) product used in the treatment of chronic hepatitis C. We share a portion of the profits on this product with Enzon Pharmaceuticals, Inc. (Enzon). We are also a party to a subsequent agreement with Roche executed in April 1999, related to further collaborative work on PEGASYS, a PEGylated interferon alfa-2a product.

PEG-INTRON® (peginterferon alfa-2b)

We entered into a manufacturing agreement with Schering-Plough Corporation in February 2000 whereby we provide one of our PEG reagents used in the manufacture of PEG-INTRON® (peginterferon alfa-2b) product used in the treatment of chronic hepatitis C.

Somavert® (pegvisomant)

We entered into a license, manufacturing, and supply agreement with Sensus Drug Development Corporation (Sensus) in January 2000, whereby we provide one of our PEG reagents used in the manufacture of Somavert® (pegvisomant), a human growth hormone receptor antagonist. In March 2001, Pharmacia Corp. (Pharmacia) acquired Sensus and in April 2003, Pfizer acquired Pharmacia. Somavert® has been approved for use in the U.S. and Europe for the treatment of certain patients with acromegaly.

Definity® (PEG)

We entered into an agreement with Dupont Pharmaceuticals, now part of Bristol Myers-Squibb Company in 1996, whereby we provide one of our PEG reagents used in the manufacture of Definity® ultrasound system designed to diagnostically visualize the heart. Definity® is the first ultrasound contrast agent in the United States that is non-blood derived.

Macugen® (pegaptanib sodium injection)

We entered into a license, manufacturing and supply agreement with Eyetech Pharmaceuticals, Inc. (Eyetech) in February 2002 whereby we provide one of our PEG reagents used in the development and commercial manufacturing of Macugen® (pegaptanib sodium injection), a PEGylated anti-Vascular Endothelial Growth Factor aptamer currently approved in the U.S. for use in treating age related macular degeneration (AMD) and for which an application for marketing approval has been filed with the EMEA by Eyetech and its partner, Pfizer. AMD is the leading cause of blindness among Americans over the age of 55. Nektar has received development milestone payments and will receive royalties on sales of commercialized products, as well as revenues from exclusive manufacturing of the PEG derivative. We will share a portion of Nektar revenues for this product with Enzon.

Macugen® is also in Phase II testing for the treatment of diabetic macular edema (DME). The FDA has granted Macugen® fast-track status for the treatment of DME.

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Selected Products in Development

Exubera® Inhaled Insulin Program

We entered into a collaborative agreement with Pfizer in January 1995 under which we are developing with Pfizer and their collaborator Sanofi-Aventis, an inhaleable version of regular human insulin (Exubera®) that can be administered systemically using our Pulmonary Technology. We believe that Exubera® could result in greater patient compliance by eliminating some insulin injections for Type 1 and some Type 2 patients and all insulin injections for some Type 2 patients.

If Exubera® is approved for commercial use, we will have the responsibility for the commercial manufacture of a portion of the inhaleable insulin drug powders and we will have the responsibility for supplying inhalers. In addition to receiving revenues for the manufacture and supply of drug powders and inhalers, we will receive a royalty on inhaleable insulin products marketed jointly by Pfizer and Sanofi-Aventis.

In November 1998, Pfizer and Aventis announced that they entered into a worldwide agreement to manufacture insulin and to co-develop and co-promote inhaleable insulin. Under the terms of the agreement, Pfizer and Aventis have constructed a jointly owned insulin manufacturing plant in Frankfurt, Germany.

In 2004, Sanofi-Synthelabo acquired Aventis to create Sanofi-Aventis. Pfizer and Sanofi-Aventis are engaged in litigation with respect to their agreement to manufacture insulin and to co-develop and co-promote inhaleable insulin. We are not a party to this litigation. There can be no assurance that this litigation will not affect the regulatory approval process or the commercialization of Exubera®.

Insulin is a protein hormone naturally secreted by the pancreas to, in part, facilitate uptake of glucose into cells. Diabetes, the inability of the body to properly regulate blood glucose levels, is caused by insufficient production of insulin by the pancreas or resistance to the insulin produced. Over time, high blood glucose levels can lead to failure of the microvascular system, which may lead to blindness, loss of circulation, kidney failure, heart disease or stroke. Insulin, in its injectable form, is supplied by various manufacturers, including Eli Lilly and Company, Novo-Nordisk A/S and Sanofi-Aventis.

According to the World Health Organization (WHO), approximately 171 million people worldwide have diabetes, and that number is expected to grow to 366 million by 2030. All Type 1 diabetics, estimated at between 5% and 10% of all diabetics, require insulin therapy. Type 1 diabetics require both basal insulin in the form of long-acting insulin and multiple treatments of regular or short-acting, insulin throughout the day. Type 2 diabetics, depending on the severity of their disease, may or may not require insulin therapy. We believe that because of the inconvenience and unpleasantness of injections, many Type 2 patients who do not require insulin to survive, despite the fact that they would benefit from it, are reluctant to start insulin treatment. Further, we believe that many Type 1 and Type 2 patients take less insulin than they should because of the dislike of injections.

A ten-year study by the National Institutes of Health (NIH) in Type 1 diabetics demonstrated that the longer term sequela of diabetes could be significantly reduced by dosing more frequently resulting in lowering of glycosolated hemoglobin. The NIH study recommended dosing regular insulin three to four times per day, a regimen that would more closely mirror the action of naturally produced insulin in non-diabetics. Because of the risk of severe hypoglycemia, this course of treatment is not recommended for children, older adults, and people with heart disease or with a history of frequent severe hypoglycemia. In addition, many patients are reluctant to increase their number of daily doses because they find

injections unpleasant and inconvenient. Similar results were demonstrated in Type 2 patients in a trial in the United Kingdom (UK).

Phase I and Phase IIa clinical trials with Exubera® indicated that inhaled insulin was absorbed systemically, reduced blood glucose levels and provided the same control of diabetes as injected insulin. In October 1996, Pfizer initiated a multi-site Phase IIb outpatient trial to include up to 240 diabetes patients, the results of which were announced in June 1998. In 70 Type 1 diabetics that were treated with either inhaled or conventional

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injected insulin therapy for three months, blood levels of hemoglobin Alc, or (HbAlc), the long-term measurement of blood glucose control, were statistically equivalent. Virtually identical results were obtained in a group of Type 2 diabetics. In September 1998, Pfizer released additional Phase II data from a study of diabetics whose blood glucose was poorly controlled by oral agents alone. In that study, patients who were given Exubera® in addition to their oral medications showed marked improvement in their blood glucose control.

In June 1999, Pfizer began dosing in Phase III clinical trials. In June 2000, Pfizer reported new data on patients using inhaled insulin therapy from a Phase II continuation, or extension, study being conducted by Pfizer and Aventis. The goal of the extension study was to determine if safety and efficacy results from previously reported short-term Phase II clinical trials could be maintained in the long term. These data showed that HbAlc remained stable in patients for up to 30 months of therapy. At the time that these were compiled, 83 patients had completed 24 months of Exubera® therapy. Further data presented indicated similar results for patients who completed 30 months of therapy.

In June 2001, Pfizer reported on data released from Phase III studies showing that more Type 2 patients who were treated with Exubera® achieved the recommended blood glucose levels than patients who received only insulin injections. In addition the frequency and nature of adverse events were comparable between groups. Patients who used Exubera® developed increased insulin antibody serum binding, but there did not appear to be any related clinical significance. Additional data released from these Phase III studies suggested that Type 1 patients using inhaled insulin multiple times a day with one bedtime long acting insulin injection achieved comparable control of blood glucose to that seen in patients receiving multiple daily insulin injections. An additional Phase III study indicated that Type 2 patients who were poorly controlled on a combination of two oral diabetes therapies demonstrated improved glycemic control and greater overall satisfaction and acceptance of therapy when Exubera® was added to their treatment regimen or when it replaced oral therapies.

In December 2001, Pfizer announced that it had decided to include an increased level of controlled, long-term safety data in any potential NDA filing with the FDA with respect to Exubera®. In May and June 2002, Pfizer and Aventis released data from Phase III studies conducted with Exubera®. The data showed that Type 2 patients, who had failed to meet recommended blood glucose levels with combination oral therapy, achieved better glycemic control with Exubera® than patients who received oral agents. In addition, the study results showed that Exubera® provides glycemic control equal to insulin injections in Type 1 patients. However, the data also indicated a small relative decrease in one of the pulmonary function tests in the Exubera® treatment group. In October 2002, Pfizer and Aventis announced that they would complete additional long-term studies already underway for Exubera® to determine whether there is clinical significance to the pulmonary function data.

In June 2003, Pfizer and Aventis released Phase III data suggesting that Exubera® may provide acceptable glycemic control to significantly more subjects than rosiglitazone in Type 2 diabetes patients not optimally controlled on diet and exercise. Rosiglitazone is an oral hypoglycemic agent used to reduce the body s resistance to the action of insulin as a way of lowering blood glucose.

In March 2004, Pfizer and Aventis announced that the EMEA had accepted the filing of a marketing authorization application for Exubera®.

In June 2004, Pfizer and Aventis announced results of long-term studies held over a period of one year which showed that patients with Type 2 diabetes taking Exubera® experienced no clinically important effect on pulmonary function compared to patients on oral-agents alone.

In September 2004, Pfizer and Sanofi-Aventis announced new data from trials where the primary objective was to assess long-term pulmonary safety showing that Exubera® was effective and well-tolerated in controlling blood glucose levels over a two-year period in patients with Type 2 diabetes. The lead study investigator concluded that these data show that small pulmonary function differences between the two groups occurred early after treatment initiation, had no identified clinical relevance, and did not progress after two years of continued inhaled insulin treatment.

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In March 2005, Pfizer and Sanofi-Aventis announced that a New Drug Application was accepted by the U.S. FDA for Exubera®. Pfizer and Sanofi-Aventis are seeking approval to market Exubera® in the U.S. for adult patients with type 1 and type 2 diabetes. Pfizer and Sanofi-Aventis announced at the same time that Exubera® has been studied in more than 3,500 patients, and in some of these patients for more than seven years.

There can be no assurance that the EMEA or FDA will approve Exubera® for marketing and there can be no assurance that Pfizer or Sanofi-Aventis will obtain approval to market Exubera® in any other markets. The failure to obtain regulatory approval of Exubera® in the EU, U.S. or any other markets would significantly harm our business including without limitation, our revenue and ability to invest in other areas of our business. Any eventual label claims for Exubera® will be subject to regulatory approval of the product and its labeling. Further, there can be no assurance that the current litigation between Sanofi-Aventis and Pfizer will not impact the process for regulatory approval of Exubera® or its commercialization.

If Exubera® were to be approved in the EU by the EMEA, there is no guarantee commercialization will take place in any given market due to certain other approvals that are required prior to commercialization such as reimbursement. If Exubera® were to be approved in the U.S. by the FDA, there is no guarantee that it will be placed on formularies by the various government agencies or other health care plans.

PEG CDP 870 (PEG-anti-TNF alpha antibody fragment) Program

We entered into a license, manufacturing and supply agreement for CDP 870 (PEG-anti-TNF alpha antibody fragment) with Celltech Group plc (Celltech) which was executed in 2000. This agreement was subsequently assigned to Pharmacia for the rheumatoid arthritis indication. In October 2002, Pharmacia initiated Phase III clinical trials with CDP 870 for rheumatoid arthritis. In April 2003, Pfizer acquired Pharmacia and in February 2004, Pfizer reassigned rights to CDP 870 back to Celltech. In 2004, Celltech was acquired in whole by UCB Pharma, a global pharmaceutical and specialty chemical company.

In March 2004, Celltech announced preliminary Phase III CDP 870 data for rheumatoid arthritis indicating that the study met its primary endpoint.

CDP 870 is also in Phase III trials as a treatment for Crohn s disease, a chronic digestive disorder of the intestines, sometimes referred to as inflammatory bowel disease.

Under the agreement for CDP 870, we receive milestone payments and PEG manufacturing revenues, and royalties on product sales, if the product is commercialized. We will share a portion of the royalties on this product with Enzon.

Although UCB Pharma has stated that they plan to develop CDP 870, there can be no assurance that they will continue the development of CDP 870 or that this product will be filed for approval or will be approved for use in the U.S., EU or other markets.

Nektar currently has product development collaborations with UCB Pharma for two other products, CDP 791 (PEG-antibody fragment angiogenesis inhibitor) and CDP 484 (PEGylated antibody fragment targeting pro-inflammatory cytokine interleukin 1-beta), both of which are

in Phase I/II clinical trials.

SprayGel (PEG-hydrogel) Program

We are a party to a license, supply and manufacturing agreement with Confluent executed in August 1999, for use of our PEG-hydrogel in Confluent s SprayGel adhesion barrier system. Under the terms of this arrangement, we manufacture and supply PEG components used in the SprayGel system and receive royalty payments on sales of commercialized products, and PEG manufacturing and supply revenues from Confluent. SprayGel was approved for commercial distribution in Europe, receiving product certification by European regulatory authorities in November 2001. In June 2002, Confluent initiated Phase II/III pivotal trials in the U.S. of SprayGel.

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SprayGel is a biodegradable, water-based, coating material designed to prevent postoperative adhesions formation. Adhesions can be responsible for severe pain and discomfort as well as small bowel obstructions and are the leading cause of infertility in women following gynecological surgery. Approximately 500,000 surgical procedures are performed annually to remove adhesions.

CERA (Continuous Erythropoiesis Receptor Activator) Program

We announced in February 2004, a collaboration with Roche whereby we had licensed a proprietary PEG (PEGylation) reagent used in the manufacture of Roche s product, Continuous Erythropoiesis Receptor Activator (CERA). Under the terms of the collaboration, we will receive milestone and manufacturing revenues during development and will receive royalty and manufacturing revenues following commercialization of the product. In March 2004, Roche announced that it had advanced CERA into Phase III trials.

CDP 791 and CDP 484 Programs

We entered into a licensing, manufacturing and supply agreement with Celltech for PEGylated antibody fragment products CDP 791 (PEG-antibody fragment angiogenesis inhibitor) and CDP 484 (PEGylated antibody fragment targeting pro-inflammatory cytokine interleukin 1-beta) for cancer and rheumatoid arthritis, respectively, in October 2002. In 2004, Celltech was acquired by UCB Pharma.

Under the terms of the agreement, we will provide exclusive development and manufacturing for each activated PEG for both products. In exchange, we will receive milestone payments, manufacturing revenues and royalties on sales of commercialized products.

In 2003, Celltech announced the initiation of a Phase I trial for CDP 791. To date, no Phase I results have been published for CDP 791.

In March 2004, Celltech announced they had initiated in late 2003 large placebo controlled Phase I/II trials in rheumatoid arthritis patients for CDP 484.

There can be no assurance that UCB Pharma will continue the development of CDP 791 or CDP 484 or that those products will be filed for approval or be approved for use in the U.S., EU or other markets. We currently have three product development partnerships with UCB Pharma (CDP 870, CDP 791 and CDP 484).

Tobramycin Inhaled Powder Program

In December 2001, we entered into a collaboration with Chiron Corporation to develop Tobramycin inhaled powder (TIP), for the treatment of *Pseudomonas aeruginosa* in cystic fibrosis patients and to explore the development of other inhaled antibiotics using our Advanced Pulmonary Technology. Chiron s existing tobramycin product, TOBI, was introduced in 1998 as the first inhaled antibiotic approved for treating Pseudomonas aeruginosa lung infections in cystic fibrosis patients.

In July 2003, Chiron initiated a Phase I trial in patients for TIP.

In October 2004, Chiron presented Phase I clinical trial data. The data presented suggest that TIP may significantly reduce the treatment burden for cystic fibrosis patients by offering a short administration time and improved portability. The Phase I trial, which included 90 patients at 15 study centers in the U.S., compared the safety, pharmacokinetics and delivery time of our dry powder TIP administered via our inhalation system to Chiron s TOBI® tobramycin solution for inhalation administered via nebulizer. Chiron also stated that it plans to initiate Phase III clinical trials for further study of TIP.

Under the terms of the tobramycin collaboration, we are responsible for the development of the formulation of inhaleable tobramycin as well as clinical and commercial manufacturing of the drug formulation and delivery

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device. Chiron is responsible for the clinical development and worldwide commercialization of the drug formulation and delivery device combination. We will receive research and development funding, milestone payments, and royalty payments and manufacturing revenues once the product is commercialized.

Inhaled Leuprolide Program

In January 2002, we announced a strategic alliance with Enzon that includes an agreement making us solely responsible for licensing Enzon s PEGylation patents, an option for Enzon to license our PEGylation patents, an agreement to explore the development of non-invasive delivery of single-chain antibody products via the pulmonary route and settlement of a patent infringement litigation originally initiated by Enzon. We will have the option to license Enzon s PEGylation patents for use in our proprietary products. Enzon will receive a royalty or a share of profits on final product sales of any products that use Enzon s patented PEG technology, including branched PEG. As part of this broad alliance, we entered into a collaboration to develop up to three products using our Pulmonary Technology and/or SCF Technology. The first potential product under this collaboration may be an inhaleable formulation of leuprolide acetate to treat endometriosis. Under the terms of this collaboration, we will be responsible for the development of drug formulations for the agreed upon pharmaceutical agents as well as clinical and commercial manufacturing of the drug formulation and delivery device. Enzon will be responsible for the clinical development and worldwide commercialization of the drug formulation and delivery device combination. We may receive research and development funding and milestone payments as the program progresses through further clinical testing, and will receive royalty payments if the product is commercialized. As part of this alliance, Enzon made a $40.0 million equity investment in our convertible preferred stock.

Inhaled MARINOL® (inhaled dronabinol) Program

In February 2002, we entered into a collaboration with Unimed (Unimed), a wholly owned subsidiary of Solvay Pharmaceuticals, Inc., (Solvay) to develop a Metered Dose Inhaler (MDI) formulation of MARINOL® (dronabinol) to be used for multiple indications. MARINOL® capsules are approved in the U.S. for the treatment of anorexia associated with weight loss in patients with AIDS and for the treatment of refractory nausea and vomiting associated with cancer chemotherapy. In the second quarter of 2003, Unimed initiated a Phase I trial.

Under the terms of the collaboration, we are responsible for development of the formulation, as well as clinical and commercial manufacturing of the drug formulation delivery and device. Solvay is responsible for the clinical development and worldwide commercialization of the drug formulation and delivery device combination. We will receive research and development funding, milestone payments as the program progresses through further clinical testing, and royalty payments on product sales and manufacturing revenues if the product is commercialized.

Dental Regeneration Products

In January 2003, we announced an agreement with the Straumann Group (Straumann) to license, manufacture and supply Nektar Advanced PEGylation Technology for the development of hydrogels for dental regeneration products. The proposed PEG-based hydrogel product will be designed for use by dentists to support tissue regeneration in dental surgery. Under the agreement, Straumann will license and source our technology and material exclusively for a proprietary formulation. We will receive milestone and manufacturing payments as well as royalties on commercialized products.

Supplemental Agreement with Alliance Pharmaceutical Corp.

In March 2002, we announced the expansion of our agreement with Alliance Pharmaceutical Corp. (Alliance) regarding the PulmoSphere® particle and particle processing technology, aspects of which we

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initially acquired from Alliance in November 1999. The PulmoSphere® technology is a particle engineering method designed to enhance the performance of drugs delivered via the lung in propellant-based metered-dose inhalers and dry powder inhalers. As a result of the supplemental agreement, we paid Alliance $5.25 million in exchange for rights beyond inhaleable applications and other considerations. In addition, we were obligated to pay Alliance future milestones and royalty payments on some products developed by us or our licensees utilizing the PulmoSphere® technology. In February 2005, we amended this agreement by agreeing to pay Alliance approximately $1.8 million in exchange for certain raw material used in our production process and the termination of all of our future royalty and payment obligations to Alliance.

Feasibility Studies

In addition to the partner collaborations mentioned above and other development programs, we have conducted and continue to conduct feasibility studies of additional drug formulations both on our own account and in cooperation with potential collaboration partners. There can be no assurance that any of our feasibility studies will be successful or result in collaborative development programs.

Collaborations Terminated in 2004

PEG CDP 860 Program

In March 2004, Celltech announced that due to their lack of progress in partnering discussions, they discontinued development of CDP 860, an antibody fragment using Nektar Advanced PEGylation Technology which was formerly in Phase II trials for cancer.

Undisclosed PEG Product

In March 2004, we ceased development of an undisclosed product in Phase II trials as a result of our partner s determination not to pursue further development.

NEKTAR PROPRIETARY PRODUCTS PROGRAMS

Approximately two years ago we began investing in our own proprietary products. Our proprietary products primarily apply our technologies to selected off-patent molecules that we believe would benefit from the application of our technologies to improve performance and/or delivery of these compounds. Our objective is to complete mid to late-stage clinical trials on these products, and then evaluate the need for a partner for late stage development efforts and/or commercialization of these products. We may also choose to partner some of our proprietary products at earlier stages of development. We believe that, when we partner these programs at a later stage, we will be able to gain a greater share of the products economics compared to partnering the products at earlier stages.

We currently have four proprietary products in the early stages of development. One of these products, an inhaled small molecule product, has entered Phase I trials and a second inhaled product is in proof-of-concept human studies. The other two products are in preclinical studies.

We believe that there may be additional off-patent or near-term patent expiration compounds that could benefit from the application of our technologies to improve such compounds performance and delivery.

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Research and Development

Our research and development activities can be divided into research and preclinical programs, clinical development programs and commercial readiness. We estimate the costs associated with research and preclinical programs, clinical development programs, and commercial readiness over the past three years to be the following (in millions):

	Years ended December 31,		
	2004	2003	2002
Research and preclinical programs	$ 37.4	$ 29.0	$ 37.6
Clinical development programs	59.4	58.0	82.4
Commercial readiness	36.7	35.1	27.6
Total	$ 133.5	$ 122.1	$ 147.6

Our portfolio of projects can be broken down into two categories: 1) partnered projects and 2) proprietary products and technology development. We estimate the costs associated with partnered projects and proprietary products and technology development to be the following (in millions):

	Years ended December 31,	
	2004	2003
Partnered projects	$ 93.2	$ 92.7
Proprietary products and technology development	40.3	29.4
Total	$ 133.5	$ 122.1

The above information is not available for the year ended December 31, 2002.

Our total research and development expenditures can be disaggregated into the following significant types of expenses (in millions):

	Years ended December 31,		
	2004	2003	2002
Salaries and employee benefits	$ 59.0	$ 57.2	$ 67.3

Outside services	28.7	21.0	21.2
Supplies	18.9	16.7	22.0
Facility and equipment	19.7	16.7	18.4
Travel and entertainment	1.9	1.5	2.1
Purchased technology			5.3
Allocated overhead	4.9	7.1	8.3
Other	0.4	1.9	3.0
Total	$ 133.5	$ 122.1	$ 147.6

Manufacturing

With respect to products based on our Pulmonary Technology, we generally plan to formulate, manufacture and package the powders for our pulmonary delivery products and to subcontract the manufacture of our pulmonary delivery devices.

Our device for use with Exubera®, the pulmonary inhaler, is still in clinical testing. Further work is underway to enable large-scale commercial manufacturing and additional work may be required to optimize the device for regulatory approval, field reliability or other issues that may be important to its commercial success. Additional design and development work may lead to a delay in regulatory approval. Under our collaborative

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agreement with Pfizer to develop Exubera®, both we and Pfizer will manufacture a portion of inhaleable insulin powders and Pfizer will be responsible for filling and packaging blisters. The terms of the supply agreement with Pfizer provide that prior to the commercialization of Exubera®, we must qualify a powder processing facility and a device manufacturer or manufacturers for Exubera®.

We have built a powder manufacturing and packaging facility in San Carlos, California capable of producing powders in quantities we believe are sufficient for clinical trials of products based on our Pulmonary Technology. This facility has been inspected and licensed by the State of California and is used to manufacture and package powders under current Good Manufacturing Practices (cGMP). If we are able to scale-up and validate the facility in time then we believe that the manufacturing capacity will be sufficient to meet initial anticipated commercial manufacturing requirements.

We have developed a high capacity automated filling technology, that when validated, we believe will be capable of filling blisters on a production scale for moderate and large volume products using our Pulmonary Technology. The technology has been transferred to Pfizer who will be responsible for commercial packaging and filling the bulk drug powders for Exubera®.

One of our proprietary pulmonary inhaler devices is being developed for commercial use and is being used in Phase III Exubera® trials. We have identified and have established formal supply agreements with contract manufacturers that we believe have the technical capabilities and production capacity to manufacture our pulmonary inhaler device. We believe that these contract manufacturers can successfully receive the device technology and knowledge transferred from our device development group, scale up the manufacturing process, and meet the requirements of cGMP. The contract manufacturers have completed construction of their facilities. Manufacturing scale-up and qualification, and validation efforts are underway. We are examining scale-up and validation plans to support their commercial operations.

In August 2000, we entered into a Manufacturing and Supply Agreement with our contract manufacturers to provide for the manufacturing of our pulmonary inhaler device for Exubera®. Under the terms of the Agreement, we may be obligated to reimburse the contract manufacturers for the actual unamortized and unrecovered portion of any equipment procured or facilities established and the interest accrued for their capital overlay in the event that Exubera® does not gain FDA approval to the extent that the contract manufacturers cannot re-deploy the assets. While such payments may be significant, at the present time, it is not possible to estimate the loss that will occur should Exubera® not be approved. We have also agreed to defend, indemnify and hold harmless the contract manufacturers from and against third party liability arising out of the agreement, including product liability and infringement of intellectual property. There is no limitation on the amount of potential future payments we could be required to make under these indemnification obligations. We have never incurred costs to defend lawsuits or settle claims related to these indemnification obligations. If any of our indemnification obligations is triggered, we may incur substantial liabilities.

With respect to products using Nektar Advanced PEGylation Technology, we have one facility in Huntsville, Alabama for the manufacture of PEG-derivatives. We are currently increasing capacity to handle current and anticipated future demand.

With respect to products using our Nektar SCF Technology, we currently have one facility in Bradford, England for the production of dry powder material meeting the requirements of current Good Manufacturing Practices.

There can be no assurance that we or our partners will be able to successfully process drug powders, or manufacture products on our autofiller system in a timely manner or at commercially reasonable cost. Any failure or delay in further developing this technology would delay product development or inhibit commercialization of our products and would have a material adverse effect on us. Moreover, there can be no assurance that we will be able to scale-up and validate our contract manufacturers successfully, or that we will be able to maintain satisfactory contract manufacturing on commercially acceptable terms. Our dependence upon

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third parties and their supply chains for the manufacture of our pulmonary inhaler device and its supply chain may adversely affect our cost of goods, our ability to develop and commercialize products on a timely and competitive basis, and the production volume of pulmonary inhaler devices.

Government Regulation

The research and development, clinical testing, manufacture and marketing of products using our technologies are subject to regulation by the FDA and by comparable regulatory agencies in other countries. These national agencies and other federal, state and local entities regulate, among other things, research and development activities and the testing (in vitro and in animals and in human clinical trials), manufacture, safety, effectiveness, labeling, storage, record keeping, approval, advertising and promotion of our products.

The process required by the FDA before a product using our technologies may be marketed in the United States depends on whether the compound has existing approval for use in other dosage forms. If the drug is a new chemical entity that has not been previously approved, the process includes the following:

- Extensive preclinical laboratory and animal testing;
- Submission of an Investigational New Drug application (IND);
- Adequate and well-controlled human clinical trials to establish the safety and efficacy of the drug for the intended indication; and
- Submission to the FDA for approval of an NDA, for drugs or a Biological License Application (BLA), for biological products.

If the drug has been previously approved, the approval process is similar, except that certain preclinical tests relating to systemic toxicity normally required for the IND and NDA application may not be necessary.

Preclinical tests include laboratory evaluation of product chemistry and animal studies to assess the potential safety and efficacy of the product and its chosen formulation. Preclinical safety tests must be conducted by laboratories that comply with FDA Good Laboratory Practices regulations. The results of the preclinical tests are submitted to the FDA as part of the IND application and are reviewed by the FDA before clinical trials can begin. Clinical trials may begin 30 days after receipt of the IND by the FDA, unless the FDA raises objections or requires clarification within that period.

Clinical trials involve the administration of the drug to healthy volunteers or patients under the supervision of a qualified, identified medical investigator according to an approved protocol. Drug products to be used in clinical trials must be manufactured according to current Good Manufacturing Practices. Clinical trials are conducted in accordance with protocols that detail the objectives of the study, the parameters to be used to monitor participant safety and efficacy or other criteria to be evaluated. Each protocol is submitted to the FDA under the original IND.

Apart from the IND submission process described above, each clinical study is conducted after written approval is obtained from an independent Institutional Review Board (IRB). The IRB considers, among other things, ethical factors, the potential risks to subjects participating in the trial and the possible liability to the institution where the trial(s) is/are being conducted. The IRB also approves the consent form signed by the trial participants.

Clinical trials are typically conducted in three sequential phases. In Phase I, the initial introduction of the drug into healthy human subjects, the product generally is tested for tolerability, pharmacokinetics, absorption, metabolism and excretion. Phase II involves studies in a limited patient population to:

Determine the efficacy of the product for specific targeted indications;

Determine dosage tolerance and optimal dosage and regimen of administration; and

Identify possible adverse effects and safety risks.

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After Phase II trials demonstrate that a product is effective and has an acceptable safety profile, Phase III trials are undertaken to evaluate the further clinical efficacy and safety of the drug/formulation within an expanded patient population at geographically dispersed clinical study sites, and in large enough trials to provide statistical proof of efficacy/tolerability. The FDA, the clinical trial sponsor, the investigators or the IRB may suspend clinical trials at any time if any one of them believes that study participants are being subjected to an unacceptable health risk.

The results of product development, preclinical studies and clinical studies are submitted to the FDA as an NDA/BLA for approval of the marketing and commercial shipment of the drug product. The FDA may deny an NDA/BLA if applicable regulatory criteria are not satisfied or may require additional clinical and/or pharmaceutical testing or requirements. Even if such data are submitted, the FDA may ultimately decide that the NDA/ BLA do not satisfy all of the criteria for approval (e.g. consistency of manufacture of the drug/formulation). Product approvals, once obtained, may be withdrawn if compliance with regulatory standards is not maintained or if safety concerns arise after the product reaches the market. The FDA may require additional post-marketing clinical testing and pharmacovigilance programs to monitor the effect of drug products that have been commercialized and has the power to prevent or limit future marketing of the product based on the results of such programs.

Each domestic drug product-manufacturing establishment must be registered with, and approved by, the FDA. Establishments handling controlled substances must in addition, be licensed by the U.S. Drug Enforcement Administration. Domestic manufacturing establishments are subject to biennial inspections by the FDA for compliance with cGMP. Facilities and drug products manufactured in the UK are also subject to European regulatory review. They are also subject to U.S., and UK federal, state and local regulations regarding workplace safety, environmental protection and hazardous and controlled substance controls, among others.

Many of the drugs we are developing are already approved for marketing by the FDA in another form and delivered by another route. We believe that when working with approved drugs, the approval process for products using our alternative drug delivery or formulation technologies may require less time and fewer tests than for new chemical entities. However, we expect that our formulations for use with any of our technologies may use excipients not currently approved for use (e.g., pulmonary delivery). Use of these excipients will require additional toxicological testing that may increase the costs of or length of time to gain regulatory approval. In addition, regulatory procedures as they relate to our products may change as regulators gain experience, and any such changes may delay or increase the cost of regulatory approvals.

For products currently under development based on our Pulmonary Technology, our pulmonary inhaler devices are considered to be part of a drug/device combination for deep lung delivery of each specific molecule. Prior to submission of an IND, the FDA will make a determination as to the most appropriate Center and Division within the FDA that will assume prime responsibility for the review of the IND and NDA/BLA. In the case of our products, the Center for Drug Evaluation and Research in consultation with the Center for Devices and Radiological Health could be involved in the review. The assessment of jurisdiction within the FDA is based upon the primary mode of action of the drug or the location of the specific expertise in one of the Centers as identified in the FDA s inter Center agreement.

To date, our partners have generally been responsible for clinical and regulatory approval procedures, but we may participate in this process by submitting to the FDA a drug master file developed and maintained by us which contains data concerning the manufacturing processes for the inhaler device or drug product. Through our internal proprietary products development efforts, we have prepared and submitted an IND application and would be responsible for additional clinical and regulatory procedures. The clinical and manufacturing development and regulatory review and approval process generally takes a number of years and requires the expenditure of substantial resources. Our ability to manufacture and sell products, whether developed by us or under collaboration agreements, ultimately depends upon the completion of satisfactory clinical trials and success in obtaining marketing approvals from the FDA and equivalent foreign health authorities.

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Sales of our products outside the U.S. are subject to local regulatory requirements governing clinical trials and marketing approvals for drugs. Such requirements vary widely from country to country.

In developing the device component for our Pulmonary Technology, we have sought to develop our quality systems and design engineering function in adherence to the principles of design control for medical devices as set forth in the applicable regulatory guidance. Although hybrid drug/device products are typically reviewed as a drug, we have sought to adhere to the design control approach both as a good business practice, and because it appears that the drug and biologic centers of the FDA and other worldwide agencies are adopting this policy. In Europe, this has already taken place and delivery devices are viewed as separate entities subject to review as such under the Medical Device Directive. In the U.S., it is our intention to comply with the FDA regulations for devices.

There can be no assurance that products that we develop, including devices designed by us and built by our contract manufacturers, will be approved, or will meet approval requirements, on a timely basis, the failure of which would have a material adverse effect on us.

Patents and Proprietary Rights

We routinely apply for patents for our innovations and for improvements to our technologies. We also rely on our trade secrets and know-how to protect our technologies and our competitive position. We plan to defend our proprietary technologies from infringement, misappropriation, duplication and discovery through our issued patents and our proprietary know-how.

Our patent portfolio contains patents and patent applications that encompass each of our technologies including Nektar Advanced PEGylation, SCF and Pulmonary technologies. Our Advanced PEGylation patents and patent applications cover reactive PEG derivatives, PEG-drug conjugates, PEG-based prodrugs and PEG-drug delivery vehicles. Our SCF patents and patent applications cover compositions and apparatuses for preparing particles using our SCF Technology. Our Pulmonary Technology patents and patent applications cover our integrated systems for pulmonary delivery of both large and small molecule drugs. Although our early Advanced PEGylation Technology patent applications were filed in the United States only, we routinely file patent applications on innovations and improvements in each of these areas on a worldwide basis. Generally, the term of a new patent is twenty years from the date on which the application for the patent was filed in the United States or, in special cases, from the date an earlier related application was filed, subject to the payment of maintenance fees.

With regard to our Advanced PEGylation Technology patent portfolio, we have filed patent applications directed to activated PEG reagents having a variety of structures (branched or multi-armed PEGs, forked PEGs, linear PEGs, etc.) and reactive groups, methods of producing highly pure polymer reagents, PEG prodrugs having hydrolysable linkages, PEG-based hydrogels and alternative gel systems and PEG conjugates of certain molecules. Patents or patent applications have issued or have been published in many of these areas.

SCF Technology involves contacting an active agent solution or suspension with a supercritical fluid to precipitate active agent particles from the solution or suspension. The patents and patent applications cover both the method of forming the particles and apparatuses for carrying out the method and are not limited to the particular product made.

Our Pulmonary Technology patent portfolio relates to pharmaceutical compositions and reagents, medical devices and equipment and methods for preparation, packaging and delivery of our pharmaceutical compositions. This portfolio involves spray drying solutions and suspensions to prepare particles of various morphologies. Patents that have issued in these areas cover our pulmonary inhaler devices, formulations for

pulmonary delivery and methods for preparing, packaging and using these formulations and particular active agent formulations for delivery via the respiratory tract.

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The patent positions of pharmaceutical, biotechnology and drug delivery companies, including ours, are uncertain and involve complex legal and factual issues. There can be no assurance that patents we apply for will be issued, or that patents that are issued will be valid and enforceable. Even if such patents are enforceable, we anticipate that any attempt to enforce our patents could be time consuming and costly. Additionally, the coverage claimed in a patent application can be significantly reduced before the patent is issued. As a consequence, we do not know whether any of our pending patent applications will be granted with broad coverage or whether the claims that eventually issue or that have issued will be circumvented. Since publication of discoveries in scientific or patent literature often lag behind actual discoveries, we cannot be certain that we were the first inventor of inventions covered by our issued patents or pending patent applications or that we were the first to file patent applications for such inventions. Moreover, we may have to participate in interference proceedings declared by the U.S. Patent and Trademark Office, which could result in substantial cost to us, even if the eventual outcome is favorable. An adverse outcome could subject us to significant liabilities to third parties, require disputed rights to be licensed from or to third parties or require us to cease using the technology in dispute.

Numerous pending and issued U.S. and foreign patent rights and other proprietary rights owned by third parties relate to pharmaceutical compositions and reagents, medical devices, and equipment and methods for preparation, packaging and delivery of pharmaceutical compositions. We cannot predict with any certainty which, if any, patent references will be considered relevant to our technology by authorities in the various jurisdictions where such rights exist, nor can we predict with certainty which, if any, of these rights will or may be asserted against us by third parties. There can be no assurance that we can obtain a license to any technology that we determine we need on reasonable terms, if at all, or that we could develop or otherwise obtain alternate technology. The failure to obtain licenses if needed would have a material adverse effect on us.

We also rely upon trade secret protection for our confidential and proprietary information. No assurance can be given that others will not independently develop substantially equivalent proprietary information and techniques or otherwise gain access to our trade secrets or disclose such technology, or that we can meaningfully protect our trade secrets.

Third parties from time to time have asserted or may assert that we are infringing their proprietary rights based upon issued patents, trade secrets or know-how that they believe cover our technology. In addition, future patents may be issued to third parties that our technology may infringe. We could incur substantial costs in defending ourselves and our partners against any such claims. Furthermore, parties making such claims may be able to obtain injunctive or other equitable relief, which could effectively block our ability to develop or commercialize some or all of our products in the United States and abroad, and could result in the award of substantial damages. In the event of a claim of infringement, we and our partners may be required to obtain one or more licenses from third parties. There can be no assurance that our partners and we will be able to obtain such licenses at a reasonable cost, if at all. Defense of any lawsuit or failure to obtain any such required license could have a material adverse effect on us.

Our ability to develop and commercialize our technologies will be affected by our or our partners access to the drugs that are to be formulated. Many biopharmaceutical drugs, including some of those that are presently under development by us, are subject to issued and pending United States and foreign patent rights which may be owned by competing entities. There can be no assurance that we or our partners will be able to provide access to drug candidates for formulation or that, if such access is provided, we or our partners will not be accused of, or determined to be, infringing a third party s rights and will not be prohibited from working with the drug or be found liable for damages that may not be subject to indemnification. Any such restriction on access or liability for damages would have a material adverse effect on us.

It is our policy to require our employees and consultants, outside scientific collaborators, sponsored researchers and other advisors who receive confidential information from us to execute confidentiality agreements upon the commencement of employment or consulting relationships with us. These agreements provide that all confidential information developed or made known to the individual during the course of the

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individual s relationship with us is to be kept confidential and not disclosed to third parties except in specific circumstances. The agreements provide that all inventions conceived by an employee shall be our property. There can be no assurance, however, that these agreements will provide meaningful protection or adequate remedies for our trade secrets in the event of unauthorized use or disclosure of such information.

Competition

We believe that products developed using our technologies will compete on the basis of one or more of the following parameters: efficacy, safety, reproducibility, patient convenience and cost. There is intense competition in each of our technology platforms including non-invasive delivery and less invasive delivery of peptides and proteins, and improved formulation and delivery of small molecules by the most common routes of delivery including pulmonary, oral, and injectable. In addition, a number of the products being developed using our technologies have direct and indirect competition from other companies including both drug delivery companies and pharmaceutical companies many of which are much larger and have more resources than we do.

With respect to Nektar Advanced PEGylation Technology, there are a number of companies developing alternative PEGylation technologies such as Dow Chemical Company, SunBio Corporation, Mountain View Pharmaceuticals, Inc., Neose, NOF Corporation, and Valentis, Inc., and there may be several chemical, biotechnology and pharmaceutical companies also developing PEGylation technologies. Indirect competitors to PEGylation for less invasive delivery of peptides and proteins include companies developing technologies for injectable controlled release such as liposomes, microparticles and hydrogels and molecule engineering approaches such as protein engineering, fusion proteins and protein glycosolation.

With respect to Nektar Pulmonary Technology, there are a number of companies developing dry powder inhalers, metered dose inhalers and liquid inhalers including nebulizers that could compete with us. Companies such as Alexza MDC, Alkermes, Inc., Aradigm Corporation, AeroGen, Inc., 3M, MannKind Corporation, Microdose Technologies Inc., Quadrant Technologies Limited, Skyepharma, and Vectura are all developing technologies that could compete with our pulmonary delivery systems.

In the non-invasive delivery of insulin, we have direct competition from companies such as Novo Nordisk, Alkermes, Inc., Microdose Technologies Inc., Quadrant Technologies Limited, and MannKind Corporation, all of which are working on pulmonary products and most with announced pharmaceutical partners. We also compete with companies such as Nobex Corporation, Emisphere Technologies, Inc., Coremed Corporation, and Generex Biotechnology Corporation, which are believed to be working on oral or buccal products for insulin delivery.

With respect to Nektar SCF Technology, there are a number of direct competitors developing competitive technology including CritiTech, Inc, Lavipharm Corp., Ferro Corporation, Ethypharm, Eiffel Technologies Limited, and others. Indirect competition for this technology comes from companies developing other ways of creating particles and improved dosage forms of small molecules for the most common routes of delivery.

For each of our technology platforms, we believe we have competitive advantages for certain applications and molecules. We monitor the competitive situation across our technology applications and products and may attempt to develop in-house, in-license or acquire technologies that improve or expand our technology platforms in order to remain competitive.

We are in competition with other drug delivery and drug discovery companies including molecule engineering companies, biopharmaceutical companies, as well as other organizations and individual inventors, many of which have resources much greater than ours including financial,

development and commercialization capabilities. Acquisition of competing companies including drug delivery companies by larger pharmaceutical companies could also enhance our competitors position. Accordingly, our competitors could succeed in developing competing technologies and products and gain regulatory approval faster than us or our partners. Development of newer technologies and products could also render our technology and products less or noncompetitive or obsolete.

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Employees and Consultants

As of December 31, 2004 we had 662 employees, of which 524 employees were engaged in research and development, including pre-commercial operations and quality activities, and 138 employees were engaged in general administration and business development. We have 312 employees who hold advanced degrees, of which 108 are Ph.D.s. None of our employees is covered by a collective bargaining agreement, and we have experienced no work stoppages. We believe that we maintain good relations with our employees.

To complement our own expertise, we utilize specialists in regulatory affairs, pulmonary toxicology, process engineering, manufacturing, quality assurance, device design, clinical trial design, and business development. These individuals include certain of our scientific advisors as well as independent consultants. See Item 10 Directors and Executive Officers of the Registrant .

General Information

We were incorporated in California in 1990 and reincorporated in Delaware in 1998. We maintain our executive offices at 150 Industrial Road, San Carlos, California 94070. Our main telephone number is (650) 631-3100.

All Nektar brand and product names that we use in connection with our company and our products are trademarks or registered trademarks of Nektar Therapeutics, in the United States and other countries. This Annual Report on Form 10-K/A, Amendment No. 1 contains additional trade names, trademarks and service marks of other companies. We do not intend our use or display of other parties trade names, or trademarks or service marks to imply a relationship with, or endorsement or sponsorship of, us by these other parties.

Available Information

We file electronically with the Securities and Exchange Commission (SEC) our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q and current reports on Form 8-K pursuant to Section 13(a) or 15(d) of the 1934 Act. The public may read or copy any materials we file with the SEC at the SEC s Public Reference Room at 450 Fifth Street, NW, Washington, DC 20549. The public may obtain information on the operation of the Public Reference Room by calling the SEC at 1-800-SEC-0330. The SEC maintains an Internet site that contains reports, proxy and information statements, and other information statements, and other information regarding issuers that file electronically with the SEC. The address of that site is *www.sec.gov*.

You may obtain a free copy of our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q and current reports on Form 8-K and amendments to those reports on the day of filing with the SEC on our website at *http://www.nektar.com*, by contacting the Investor Relations Department at our corporate offices by calling (650) 631-3100 or by sending an e-mail message to *investors@nektar.com*. The contents of our website are not part of the Annual Report on Form 10-K.

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RISK FACTORS

The following section should be read carefully in connection with evaluating our business. Any of the following factors could materially and adversely affect our business, financial position or results of operations.

If the collaborative partners we depend on to obtain regulatory approvals for and commercialize our products are not successful, or if such collaborations fail, then the product development or commercialization of our products may be delayed or unsuccessful.

When we sign a collaborative development agreement or license agreement to develop a product with a drug or biotechnology company, the drug or biotechnology company is generally expected to:

- synthesize active pharmaceutical ingredients to be used as medicines;
- design and conduct large scale clinical studies;
- prepare and file documents necessary to obtain government approval to sell a given drug product; and/or
- market and sell our products when and if they are approved.

Reliance on collaborative relationships poses a number of risks, including:

- the potential inability to control whether and the extent to which our collaborative partners will devote sufficient resources to our programs or products;
- disputes which may arise in the future with respect to the ownership of rights to technology and/or intellectual property developed with collaborative partners;
- disagreements with collaborative partners which could lead to delays in or termination of the research, development or commercialization of product candidates, or result in litigation or arbitration;
- the potential for contracts with our collaborative partners to fail to provide significant protection or to be effectively enforced if one of these partners fails to perform. Collaborative partners have considerable discretion in electing whether to pursue the development of any additional products and may pursue alternative technologies or products either on their own or in collaboration with our competitors;
- the potential for collaborative partners with marketing rights to choose to devote fewer resources to the marketing of our products than they do to products of their own development;

risks related to the ability of our collaborative partners to pay us; and

the potential for collaborative partners to terminate their agreements with us unilaterally for any or no reason.

Given these risks, there is a great deal of uncertainty regarding the success of our current and future collaborative efforts.

We have entered into collaborations in the past that have been subsequently terminated. If other collaborations are suspended or terminated, our ability to commercialize certain other proposed products could also be negatively impacted. If our collaborations fail, our product development or commercialization of products could be delayed and our financial position and results of operations would be significantly harmed.

If the FDA does not timely approve the NDA filed for Exubera®, if the EMEA does not timely approve a marketing authorization application for Exubera®, or if our collaboration with Pfizer is discontinued prior to the commercial launch of Exubera®, then our financial position and results of operations will be significantly harmed.

We are developing with Pfizer an inhaleable version of insulin, Exubera®, for the treatment of Type 1 and Type 2 diabetes that will be administered using our Pulmonary Technology. Exubera® is currently in extended

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Phase III clinical trials. We currently depend on Pfizer as the source of a significant portion of our revenues. For both of the years ended December 31, 2004 and 2003, revenue from Pfizer accounted for 61% of our total revenue. On March 2, 2005, Pfizer and Sanofi-Aventis jointly announced that the FDA has accepted the filing of an NDA for Exubera®. In March 2004, Pfizer and Sanofi-Aventis announced that the EMEA has accepted the filing of a marketing authorization application for Exubera®. However, there can be no assurance that Exubera® will be approved for marketing and/or commercial use in the U.S. or E.U. Among the factors that may delay the approval of the NDA, the approval by the EMEA to market Exubera® in the E.U., or the commercial launch of Exubera® in the U.S. or the E.U., or that may impact a decision to proceed at all with respect to any of the foregoing, are the following:

- Pfizer is currently conducting studies to generate controlled long-term safety data with respect to Exubera®, in particular its effect on lung function, and the results of the studies may impact regulatory approvals.

- We and/or Pfizer may experience difficulties with respect to the processing of the dry powder formulation of inhaleable insulin and the filling and packaging of the inhaleable insulin powder for the large-scale commercial production of Exubera®.

- We, with our contract manufacturers, may experience difficulties with respect to the production of the pulmonary inhaler device for Exubera®, including the design, scale-up and automation of the commercial manufacture of the pulmonary inhaler device for Exubera®, and any such difficulties may delay the filing and approval of the NDA or the approval to market in the E.U. Our contract manufacturers may also experience difficulties with respect to manufacturing the device in high volumes for commercial use.

- Pfizer may elect for marketing or other reasons, to delay or not proceed with the commercial launch of Exubera®, once approved.

If the approval by the FDA of the NDA is substantially delayed beyond the internal estimates we have made for purposes of budgeting and resource allocation, we may not have the financial ability to continue supporting the Exubera® program or be able to meet our contractual obligations relating to the commercial launch of Exubera®. In the event of any such delay, we may also elect to divert resources away from Exubera® related activities or otherwise reduce our activities relating to the Exubera® program. Any material delay in receiving regulatory approval (which in some countries includes pricing approval), or failure to receive regulatory approval for Exubera® at all, would affect our contract research revenue from Pfizer, may result in the payment by us of substantial reimbursements to the contract manufacturers of our proprietary inhaler device with respect to the capital they have deployed in support of such activity, and would significantly harm our financial position and results of operations. Furthermore, should the collaboration with Pfizer be discontinued, our financial position and results of operations will be significantly harmed.

In December 2004, Sanofi-Aventis, Pfizer s partner, announced that its stockholders had approved all resolutions relating to the proposed merger of Sanofi-Aventis, Pfizer s partner with respect to the manufacture, co-development, and co-marketing of Exubera®, with and into Sanofi-Aventis. As a consequence of the merger, the agreement by and between Pfizer and Sanofi-Aventis is being challenged and is the subject of litigation. Although we are not a party to this litigation, any disruption or delays to the Exubera® program could adversely affect the ability to market this product if and when it is approved for use, which would materially and adversely impact our business.

If we fail to establish future successful collaborative relationships, then our financial results may suffer and our product development efforts may be delayed or unsuccessful.

We intend to seek future collaborative relationships with pharmaceutical and biotechnology partners to fund some of our research and development expenses and to develop and commercialize potential products. Further, we anticipate that the timing of drug development programs under existing collaborative agreements with our

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partners will continue to affect our revenues from such agreements. We may not be able to negotiate acceptable collaborative arrangements in the future, and any arrangements we do negotiate may not be successful. If we fail to establish additional collaborative relationships, we will be required to undertake research, development, marketing, and manufacturing of our proposed products at our own expense or discontinue or reduce these activities.

Our increasing investment in the development and commercialization of new products prior to seeking collaborative arrangements may be unsuccessful and adversely impact our operating results, financial condition, and liquidity.

We intend to fund significant development expenses associated with the development and commercialization of new products, including clinical trials, developed through our Proprietary Products Group prior to seeking collaborative relationships with pharmaceutical and biotechnology partners. While we believe this strategy may result in improved economics for any products ultimately developed and approved, it will require us to invest significant funds in developing these products without reimbursement from a collaborative partner. If we are ultimately not able to negotiate acceptable collaborative arrangements with respect to these products, or any arrangements we do negotiate are not successful, we will not receive an adequate return on these investments and our operating results and financial condition would suffer. Even if our development efforts are ultimately acceptable, our increased investment in the development of these products could adversely impact our results of operations and liquidity prior to their commercialization.

If our drug delivery technologies are not commercially feasible, then our revenues and results of operations will be impacted negatively.

We are in an early stage of development with respect to most of our products. There is a risk that our technologies will not be commercially feasible. Even if our technologies are commercially feasible, they may not be commercially accepted across a range of large and small molecule drugs. None of the products using our Pulmonary Technology has been approved for use. Although our Advanced PEGylation Technology has been incorporated in six products most of the products incorporating this technology are still in clinical trials. Our Supercritical Fluid Technology is primarily in an early stage of feasibility testing. Our potential products require extensive research, development and preclinical and clinical testing. Our potential products also may involve lengthy regulatory reviews and require regulatory approval before they can be sold. We do not know if, and cannot provide assurance that, any of our potential products will prove to be safe and effective, accomplish the objectives that we or our collaborative partners are seeking through the use of our technologies, meet regulatory standards or continue to meet such standards if already approved. There is a risk that we, or our collaborative partners, may not be able to produce any of our potential products in commercial quantities at acceptable costs, or market them successfully. Failure to achieve commercial feasibility, demonstrate safety, achieve clinical efficacy, obtain regulatory approval for, or successfully market products will negatively impact our revenues and results of operations.

If our research and development efforts are delayed or unsuccessful, then we will experience delay or be unsuccessful in having our products commercialized, and our business will suffer.

Except for products using our Advanced PEGylation Technology that have already been approved by the FDA or other regulatory agencies, our product candidates are still in research and development, including preclinical testing and clinical trials. Preclinical testing and clinical trials are long, expensive and uncertain processes. It may take us, or our collaborative partners, several years to complete this testing, and failure can occur at any stage in the process. Success in preclinical testing and early clinical trials does not ensure that later clinical trials will be successful. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in later stage clinical trials, even after promising results in earlier trials.

Any clinical trial may fail to produce results satisfactory to us, our collaborative partners, the FDA, or other regulatory authorities. Preclinical and clinical data can be interpreted in different ways, which could delay, limit

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or prevent regulatory approval or commercialization. Negative or inconclusive results or adverse medical events during a clinical trial could cause a clinical trial to be repeated or a program to be terminated. We typically rely on collaborative partners and third-party clinical investigators to conduct clinical trials of our products and, as a result, we may face additional delaying factors outside our control.

We do not know if any of our research and development efforts, including preclinical testing or clinical trials, will adhere to our planned schedules or be completed on a timely basis or at all. Typically, there is a high rate of attrition for product candidates in preclinical and clinical trials.

If our drug delivery technologies do not satisfy certain basic feasibility requirements such as total system efficiency, then our products may not be competitive.

We may not be able to achieve the total system efficiency for products based on our Pulmonary Technology that is needed to be competitive with alternative routes of delivery or formulation technologies. We determine total system efficiency by the amount of drug loss during manufacture, in the delivery system, and in reaching the ultimate site at which the drug exhibits its activity. We would not consider a drug to be a good candidate for development and commercialization using our Pulmonary Technology if drug loss is excessive at any one stage or cumulatively in the manufacturing and delivery process.

Our ability to efficiently attach PEG polymer chains to a drug molecule is the initial screen for determining whether drug formulations using our Advanced PEGylation Technology are commercially feasible. We would not consider a drug formulation to be a good candidate for development and commercialization using our Advanced PEGylation Technology if we could not efficiently attach a PEG polymer chain to such drug without destroying the drug s activity.

For our Supercritical Fluid Technology, solubility characteristics of a drug and the solvents, which may be incorporated in the manufacturing process, provide the initial screen for whether drug formulations using this technology are commercially feasible. We would not consider a drug to be a good candidate for this technology if its solubility characteristics were such that the application of our technology results in very low efficiency in manufacturing of drug powders.

If our drug formulations are not stable, then we will not be able to develop or commercialize products.

We may not be able to identify and produce powdered or other formulations of drugs that retain the physical and chemical properties needed to work effectively with our inhaler devices for deep lung delivery using our Pulmonary Technology, or through other methods of drug delivery using our Advanced PEGylation or Supercritical Fluid Technologies. Formulation stability is the physical and chemical stability of the drug over time and under various storage, shipping and usage conditions. Formulation stability will vary with each drug formulation and the type and amount of ingredients that are used in the formulation. Since our drug formulation technology is new and largely unproven, we do not know if our drug formulations will retain the needed physical and chemical properties and performance of the drugs. Problems with formulated drug powder stability in particular would negatively impact our ability to develop products based on our Pulmonary Technology or Supercritical Fluid Technology, or obtain regulatory approval for or market such products.

If our drug delivery technologies are not safe, then regulatory approval of our (or our partners) products may not be obtained, or our (or our partners) products may not be developed or marketed of our (or our partners) products may be suspended following

commercialization.

We, or our collaborative partners, may not be able to prove that potential products using our drug delivery technologies are safe. Our products require lengthy laboratory, animal and human testing. We cannot be certain that these products, and our technology that developed these products, are safe or will not produce unacceptable adverse side effects. The safety of our formulations will vary with each drug and the ingredients used in our

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formulation. If any product is found not to be safe, the product will not be approved for marketing or commercialization. In addition, even if a product is approved and commercialized, regulatory authorities could still later suspend or terminate the license to market the product if it is determined that the product does not meet safety or other standards.

If product liability lawsuits are brought against us, we may incur substantial liabilities.

The manufacture, testing, marketing and sale of medical products entail an inherent risk of product liability. If product liability costs exceed our liability insurance coverage, we may incur substantial liabilities. Whether or not we were ultimately successful in product liability litigation, such litigation would consume substantial amounts of our financial and managerial resources, and might result in adverse publicity, all of which would impair our business. We may not be able to maintain our clinical trial insurance or product liability insurance at an acceptable cost, if at all, and this insurance may not provide adequate coverage against potential claims or losses.

If the products using our Pulmonary Technology do not provide consistent doses of medicine, then we will not be able to develop, and we or our partners will not be able to obtain regulatory approval for and commercialize products.

We may not be able to provide reproducible dosing of stable formulations of drug compounds. Reproducible dosing is the ability to deliver a consistent and predictable amount of drug into the bloodstream over time both for a single patient and across patient groups. Reproducible dosing of drugs based on our Pulmonary Technology requires the development of:

- an inhalation or other device that consistently delivers predictable amounts of dry powder to the deep lung;
- accurate unit dose packaging of dry powder; and
- moisture resistant packaging.

Since our Pulmonary Technology is still in development and is yet to be used in commercialized products, we cannot be certain that we will be able to develop reproducible dosing of any potential product.

If we or our partners do not obtain regulatory approval for our products on a timely basis, then our revenues and results of operations may be affected negatively.

There is a risk that we, or our partners, will not obtain regulatory approval (which in some countries includes pricing approval) for unapproved products on a timely basis, or at all. Unapproved products must undergo rigorous animal and human testing and an extensive FDA mandated or equivalent foreign authorities review process. This process generally takes a number of years and requires the expenditure of substantial resources. The time required for completing such testing and obtaining such approvals is uncertain. The FDA and other U.S. and foreign regulatory agencies also have substantial discretion to terminate clinical trials, require additional testing, delay or withhold registration and marketing approval and mandate product withdrawals including recalls. Even though our partners have obtained regulatory approval for some of our products, these products and our manufacturing processes are subject to continued review by the FDA and other regulatory authorities. Even

if we or our partners receive regulatory approval of a product, the approval may limit the indicated uses for which the product may be marketed. In addition, any marketed products and manufacturing facilities used in the manufacture of such products will be subject to continual review and periodic inspections. Later discovery from such review and inspection of previously unknown problems may result in restrictions on marketed products or on us, including withdrawal of such products from the market. The failure to obtain timely regulatory approval of products, any product marketing limitations or a product withdrawal would negatively impact our revenues and results of operations.

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In addition, we may encounter delays or rejections based upon changes in FDA regulations or policies, including policies relating to cGMP, during the period of product development. We or our partners may encounter similar delays in other countries.

If our technologies cannot be integrated successfully to bring products to market, then our or our partners ability to develop, obtain approval for, or market products, may be delayed or unsuccessful.

We may not be able to integrate all of the relevant technologies to provide complete drug delivery and formulation systems. In particular, our development of drugs based on our Pulmonary Technology relies upon the following several different but related technologies:

- dry powder formulations;
- dry powder processing technology;
- dry powder packaging technology; and
- deep lung delivery devices.

Our other technologies may face similar challenges relating to the integration of drug formulation, processing, packaging and delivery device technologies. At the same time we or our partners must:

- perform laboratory, pre-clinical, and clinical testing of potential products; and
- scale-up manufacturing processes.

All of these steps must be accomplished without delaying any aspect of product development. Any delay in one component of product or business development could delay our or our partners ability to develop, obtain approval for, or market products using our delivery and formulation technologies.

If we are not able to manufacture our products in commercially feasible quantities or at commercially feasible costs, then our products will not be successfully commercialized.

Nektar Advanced PEGylation Technology and Supercritical Fluid Technology

We are currently expanding our Advanced PEGylation Technology manufacturing capacity and anticipate having to add additional Supercritical Fluid Technology manufacturing capacity. If we are not able to scale-up to large clinical trials or commercial manufacturing for products incorporating either of these technologies in a timely manner or at a commercially reasonable cost, we risk not meeting our customers supply requirements or our contractual obligations. Our failure to solve any of these problems could delay or prevent late stage clinical testing, regulatory approval for, and commercialization of our products and could negatively impact our revenues and results of operations.

Production problems encountered during the second and third quarters of 2004 resulted in the temporary shutdown of our manufacturing facility with respect to our Advanced PEGylation products. This resulted in a decrease in product revenues and gross margin compared to 2003. Although we believe we have addressed these manufacturing problems, our failure to satisfactorily address these issues or additional production problems may negatively impact our product revenues and results of operations in future periods.

Nektar Pulmonary Technology

The manufacture of products using Nektar Pulmonary Technology involves multiple processes, all of which involve substantial risk.

Powder Processing. We have no experience manufacturing powder products for commercial purposes. With respect to drugs based on our Pulmonary Technology, we have only performed powder processing on the scale

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needed for testing formulations, and for early stage and larger clinical trials. We may encounter manufacturing and control problems as we attempt to scale-up powder processing facilities. We may not be able to achieve such scale-up in a timely manner or at a commercially reasonable cost, if at all, and the powder processing system we implement may not be applicable for other drugs. Our failure to solve any of these problems could delay or prevent some late stage clinical testing and commercialization of our products and could negatively impact our revenues and results of operations.

To date, we rely primarily on two particular methods of powder processing. There is a risk that these technologies will not work with all drugs or that the cost of drug production with this processing will preclude the commercial viability of certain drugs. Additionally, there is a risk that any alternative powder processing methods we may pursue will not be commercially practical for aerosol drugs or that we will not have, or be able to acquire the rights to use, such alternative methods.

Powder Packaging. Our fine particle powders and small quantity packaging utilized for drugs based on our Pulmonary Technology require special handling. We have designed and qualified automated filling equipment for small and moderate quantity packaging of fine powders. We face significant technical challenges in scaling-up an automated filling system that can handle the small dose and particle sizes of our powders in commercial quantities. There is a risk that we will not be able to scale-up our automated filling equipment in a timely manner or at commercially reasonable costs. Any failure or delay in such scale-up would delay product development or bar commercialization of products based on our Pulmonary Technology and would negatively impact our revenues and results of operations.

There can be no assurance we will be able to manufacture products on our autofiller system in a timely manner or at a commercially reasonable cost; any delay or failure in further developing such technology would delay product development or inhibit commercialization of our products and would have a materially adverse effect on us.

Nektar Pulmonary Inhaler Device. We face many technical challenges in developing our pulmonary inhaler device to work with a broad range of drugs, to produce such devices in sufficient quantities, and to adapt the devices to different powder formulations. Our pulmonary inhaler device being used with Exubera® is still in clinical testing. Additional design and development work may be required to optimize the device for regulatory approval, field reliability, or other issues that may be important to its commercial success.

Additional design and development work may lead to a delay in regulatory approval for any product that incorporates the device. In addition, we are attempting to develop a smaller inhaler device, which presents particular technical challenges. There is a risk that we will not successfully achieve any of these challenges. Our failure to overcome any of these challenges would negatively impact our revenues and results of operations.

For late stage clinical trials and initial commercial production, we intend to use one or more contract manufacturers to produce our pulmonary inhaler devices. There is a risk that we will not be able to maintain arrangements with our contract manufacturers on commercially acceptable terms or at all, or effectively scale-up production of our pulmonary inhaler devices through contract manufacturers. Our failure to do so would negatively impact our revenues and results of operations. Dependence on third parties for the manufacture of our pulmonary inhaler devices and their supply chain may adversely affect our cost of goods and ability to develop and commercialize products on a timely or competitive basis. Because our manufacturing processes and those of our contract manufacturers are very complex and subject to lengthy governmental approval processes, alternative qualified production sources or capacity may not be available on a timely basis or at all. Disruptions or delays in our manufacturing processes or those of our contract manufacturers for existing or new products could result in increased costs, loss of revenues or market share, or damage to our reputation.

In August 2000, we entered into a Manufacturing and Supply Agreement with our contract manufacturers to provide for the manufacturing of our pulmonary inhaler device for Exubera®. Under the terms of the Agreement,

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we may be obligated to reimburse the contract manufacturers for the actual unamortized and unrecovered portion of any equipment procured or facilities established and the interest accrued for their capital overlay in the event that Exubera® does not gain FDA approval to the extent that the contract manufacturers cannot re-deploy the assets. While such payments may be significant, at the present time, it is not possible to estimate the loss that will occur should Exubera® not be approved. We have also agreed to defend, indemnify and hold harmless the contract manufacturers from and against third party liability arising out of the agreement, including product liability and infringement of intellectual property. There is no limitation on the potential amount of future payments we could be required to make under these indemnification obligations. If any of our indemnification obligations is triggered, we may incur substantial liabilities.

There is no assurance that devices designed by us and built by contract manufacturers will be approved or will meet approval requirements on a timely basis or at all, or that any of our device development will be successful or commercially viable.

If Pfizer is not able to fill the bulk drug powders for Exubera® in commercially feasible quantities, then Exubera® will not be successfully commercialized and would negatively impact our revenues and results of operations.

We have developed a high capacity automated filling technology, which when validated, we believe will be capable of filling blisters on a production scale for moderate and large volume products using our Pulmonary Technology. The high capacity automated filling technology has been transferred to Pfizer who will have the responsibility of packaging and filling the bulk drug powders for Exubera®. There are significant technical challenges in scaling-up an automated filling system that can handle the small dose and particle sizes of our powders in commercial quantities. In addition, there is the additional risk that Pfizer has no backup manufacturing facility for this process. Any failure or delay in the manufacturing facility or process would delay product development or bar commercialization of Exubera® and would negatively impact our revenues and results of operations.

If we are not able to manufacture our dry powder inhaler device in commercially feasible quantities or at commercially feasible costs, then our Pulmonary Technology products may not be successfully commercialized.

In addition to our inhaler device being used with Exubera®, we are developing a breath actuated compact dry powder inhaler device (DPI). We are developing the DPI device to be appropriate for the delivery of either large or small molecules for short-term use. We face many unique technical challenges in developing the DPI device to work with a broad range of drugs, producing the DPI device in sufficient quantities and adapting the DPI device to different powder formulations. Our DPI device is still in clinical testing and production scale-up work is ongoing. Further design and development will be required to obtain regulatory approval for the DPI device, enable commercial manufacturing, insure field reliability or manage other issues that may be important to its commercial success. Such additional design and development work may lead to a delay in efforts to obtain regulatory approval for any product that incorporates the DPI device, or could delay the timeframe within which the device could be ready for commercial launch. There is a risk that we will not successfully achieve any of these challenges. Our failure to overcome any of these challenges would negatively impact our revenues and results of operations.

We depend on sole or exclusive suppliers for our pulmonary inhaler devices, bulk active pharmaceutical ingredients and PEG polymer chains and if such suppliers fail to supply when required, then our product development efforts may be delayed or unsuccessful and our commercial supply obligations may be compromised.

We agreed to subcontract the manufacture of our pulmonary inhaler devices used with Exubera® before commercial production. We have identified contract manufacturers that we believe have the technical capabilities

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and production capacity to manufacture such device and which can meet the requirements of cGMP. We are not certain that we will be able to maintain satisfactory contract manufacturing on commercially acceptable terms, if at all. Our failure to maintain ongoing commercial relationships with our existing contract manufacturers may subject us to significant reimbursement obligations upon termination of such relationships. Our dependence on third parties for the manufacture of our pulmonary inhaler devices may negatively impact our cost of goods and our ability to develop and commercialize products based on our Pulmonary Technology on a timely and competitive basis.

For the most part, we obtain the bulk active pharmaceutical ingredients we use to manufacture products using our technologies from sole or exclusive sources of supply. For example, with respect to our source of bulk insulin, we have entered into a collaborative agreement with Pfizer that has, in turn, entered into an agreement with Sanofi-Aventis to manufacture regular human insulin. Under the terms of their agreement, Pfizer and Sanofi-Aventis agreed to construct a jointly owned manufacturing plant in Frankfurt, Germany. Until needed, Pfizer will provide us with insulin from Sanofi-Aventis s existing plant. We obtain our supply of PEG polymer chains that we use in our products that incorporate our Advanced PEGylation Technology from a single supplier. If our sole or exclusive source suppliers fail to provide either active pharmaceutical ingredients or PEGylation materials in sufficient quantities when required, our revenues and results of operations may be negatively impacted.

If the market does not accept products using our drug delivery technologies, then our revenues and results of operations will be adversely affected.

The commercial success of our potential products depends upon market acceptance by health care providers, third-party payors like health insurance companies and Medicare and patients. Our products under development use new drug delivery technologies and there is a risk that the market will not accept our potential products. Market acceptance will depend on many factors, including:

- the safety and efficacy of products demonstrated in clinical trials;
- favorable regulatory approval and product labeling;
- the frequency of product use;
- the ease of product use;
- the availability of third-party reimbursement;
- the availability of alternative technologies; and
- the price of our products relative to alternative technologies.

There is a risk that health care providers, patients or third-party payors will not accept products using our drug delivery and formulation technologies. If the market does not accept our potential products, our revenues and results of operations would be significantly and negatively impacted.

If our products are not cost effective, then government and private insurance plans may not pay for them and our products may not be widely accepted, which will adversely affect our revenues and results of operations.

In both domestic and foreign markets, sales of our products under development will depend in part upon pricing approvals by government authorities and the availability of reimbursement from third-party payors, such as government health administration authorities, managed care providers, private health insurers and other organizations. In addition, such third-party payors are increasingly challenging the price and cost effectiveness of medical products and services. Significant uncertainty exists as to the pricing approvals for, and the reimbursement status of, newly approved health care products. Moreover, legislation and regulations affecting the pricing of pharmaceuticals may change before regulatory agencies approve our proposed products for

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marketing. Adoption of such legislation and regulations could further limit pricing approvals for, and reimbursement of, medical products. A government or third-party payor decision not to approve pricing for, or provide adequate coverage and reimbursements of, our products would limit market acceptance of such products.

If our competitors develop and sell better drug delivery and formulation technologies, then our products or technologies may be uncompetitive or obsolete and our revenues and results of operations will be adversely affected.

We are aware of other companies engaged in developing and commercializing drug delivery and formulation technologies similar to our technologies. Some of our competitors with regard to our Pulmonary Technology include Alexza MDC, Alkermes, Inc., Aradigm Corporation, AeroGen, Inc., 3M, MannKind Corporation, Microdose Technologies Inc., Quadrant Technologies Limited, Skyepharma, and Vectura. In the non-invasive delivery of insulin, we have direct competition from companies such as Aradigm Corporation, Alkermes, Inc., Microdose Technologies Inc., Quadrant Technologies Limited, and MannKind Corporation, all of which are working on pulmonary products and most with announced pharmaceutical partners. Our competitors with regard to our Advanced PEGylation Technology include Dow Chemical Company, SunBio Corporation, Mountain View Pharmaceuticals, Inc., Neose, NOF Corporation, and Valentis, Inc., and there may be several chemical, biotechnology and pharmaceutical companies also developing PEGylation technologies. Some of our competitors with regard to our Supercritical Fluid Technology include Alkermes, Battelle Memorial Institute, Ethypharm SA, Ferro Corp., Lavipharm SA and RxKinetics. Some of these companies license or provide the technology to other companies, while others are developing the technology for internal use. Many of these companies have greater research and development capabilities, experience, manufacturing, marketing, financial and managerial resources than we do and represent significant competition for us. Acquisitions of or collaborations with competing drug delivery companies by large pharmaceutical or biotechnology companies could enhance our competitors financial, marketing and other resources. Accordingly, our competitors may succeed in developing competing technologies, obtaining regulatory approval for products or gaining market acceptance before us. Developments by others could make our products or technologies uncompetitive or obsolete. Our competitors may introduce products or processes competitive with or superior to our products or processes.

If any of our pending patent applications do not issue or following issuance are deemed invalid or if any of our patents are deemed invalid, we may lose valuable intellectual property protection. If any of our products infringe third-party intellectual property rights, we may suffer adverse effects to our ability to develop and commercialize products and to our revenues and results from operations.

We have filed patents applications (and we plan to file additional patent applications) covering, among other things, aspects of: (a) our Pulmonary Technology (in general and as it relates to specific molecules) including, without limitation, our powder processing technology, our powder formulation technology, and our inhalation device technology; (b) our Advanced PEGylation Technology; and (c) our Supercritical Fluid Technology. As of December 31, 2004, we owned 825 issued U.S. and foreign patents that cover various aspects of our technologies, and we have a number of patent applications pending.

Access, or our partners access, to drugs to be formulated using our various delivery technologies affects our ability to develop and commercialize our technologies. We intend generally to rely on the ability of our partners to provide access to drugs that we formulate for pulmonary and other forms of delivery. There is a risk that our partners will not be able to provide access to such drugs. This situation is complex, and as such, the ability of any one company, including us, to commercialize a particular drug is unpredictable.

In addition, formulations of drugs that are presently under development by us, as well as our drug formulation and delivery technologies, may be subject to issued U.S. and foreign patents (and may be subject in the future to patents that issue from pending patent applications) owned by competitors. Therefore, even if our partners provide access to drugs for the formulation of pulmonary and other forms of delivery, there is a risk that third parties will accuse, and possibly a court or a governmental agency will determine, that we and/or our

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partners infringe third party patent rights covering such drugs and/or the formulation or delivery technologies utilizing such drugs, and we will be prohibited from working with the drug or formulation or delivery technology, or we will be found liable for damages that may not be subject to indemnification, or we may elect to pay such third party royalties under a license to such patent rights if one is available. Any such restrictions on access to drugs, liability for damages, prohibition, or payment of royalties would negatively impact our revenues and results of operations.

We may incur material litigation costs, which may adversely affect our business and results of operations.

On September 3, 2004, a purported securities class action complaint styled *Norman Rhodes, et al. v. Nektar Therapeutics, Ajit Gill, J. Milton Harris, and Robert B Chess,* Case No. C 04-03735 JSW, was filed in the United States District Court for the Northern District of California against Nektar Therapeutics (the Company) and certain of its current officers and directors. The complaint alleges violations of Sections 10(b) and 20(a) of the Securities Exchange Act of 1934, and Rule 10b-5. The plaintiff seeks to represent a putative class of all purchasers of the Company s securities between March 4, 2004 and August 4, 2004 (the Class Period). The complaint generally alleges that, during that Class Period, the Company and the individual defendants made false or misleading statements in certain press releases regarding Exubera®. The Complaint seeks unspecified monetary damages and other relief against all defendants. One motion for appointment of a lead plaintiff has been filed, and that motion is pending. The action is in a very early stage, and defendants have not responded to the complaint.

This litigation may be costly and could prove to be time consuming and disruptive to normal business operations. There can be no assurance that we will prevail or that the cost of defending these lawsuits will be covered by our insurance policies. While it is not possible to predict accurately or to determine the eventual outcome of this litigation, an unfavorable outcome or settlement of this litigation could have a material adverse effect on our financial position, liquidity or results of operations.

From time to time, we are party to various other litigation matters, including several that relate to our patent and intellectual property rights. We cannot predict with certainty the eventual outcome of any pending litigation or potential future litigation, and we might have to incur substantial expense in defending these or future lawsuits or indemnifying third parties with respect to the results of such litigation.

If earthquakes, tornadoes, hurricanes and other catastrophic events strike, our business may be negatively affected.

Our corporate headquarters, including a substantial portion of our research and development operations, are located in the San Francisco Peninsula, a region known for seismic activity. A significant natural disaster such as an earthquake could have a material adverse impact on our business, operating results, and financial condition. There are no backup facilities for some of our manufacturing operations located in the San Francisco Peninsula. Certain of our other facilities, such as our facility in Huntsville, Alabama and certain of our collaborative partners located elsewhere may also be subject to catastrophic events such as hurricanes and tornadoes, any of which could have a material adverse effect on our business, operating results, and financial condition.

Investors should be aware of industry-wide risks, which are applicable to us and may affect our revenues and results of operations.

In addition to the risks associated specifically with us described above, investors should also be aware of general risks associated with drug development and the pharmaceutical and biotechnology industries. These include, but are not limited to:

changes in and compliance with government regulations;

handling and disposal of hazardous materials;

workplace health and safety requirements;

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hiring and retaining qualified people; and

insuring against product liability claims.

If we do not generate sufficient cash flow through increased revenues or raising additional capital, then we may not be able to meet our substantial debt obligations.

As of December 31, 2004, we had approximately $173.9 million in long-term convertible subordinated notes and debentures, $23.6 million in non-current capital lease obligations, and $22.3 million in other long-term debt. Our substantial long-term indebtedness, which totaled $219.8 million as of December 31, 2004, has and will continue to impact us by:

making it more difficult to obtain additional financing; and

constraining our ability to react quickly in an unfavorable economic climate.

Currently we are not generating positive cash flow. Delay in the approval of Exubera®, or other adverse occurrences related to our product development efforts will adversely impact our ability to meet our obligations to repay the principal amounts on our convertible subordinated notes and debentures when due. In addition, if the market price of our common stock is below the related conversion price, the holders of the related outstanding convertible subordinated notes and debentures will not likely convert such securities to equity in accordance with their existing terms. If we are unable to satisfy our debt service requirements, substantial liquidity problems could result. As of December 31, 2004 we had cash, cash equivalents and short-term investments valued at approximately $418.7 million. We expect to use a substantial portion of these assets to fund our on-going operations over the next few years. As of December 31, 2004, we had approximately $173.9 million outstanding convertible subordinated notes and debentures, all of which will mature in 2007. We may not generate sufficient cash from operations to repay our convertible subordinated notes and debentures or satisfy any other of these obligations when they become due and may have to raise additional funds from the sale of equity or debt securities or otherwise restructure our obligations in order to do so. There can be no assurance that any such financing or restructuring will be available to us on commercially acceptable terms, if at all.

If we cannot raise additional capital our financial condition may suffer.

Our capital needs may change as a result of numerous factors, and may result in additional funding requirements. In addition, we may choose to raise additional capital due to market conditions or strategic considerations. To the extent that additional capital is raised through the sale of equity or convertible debt securities, the issuance of such securities could result in dilution to our stockholders.

We have no material credit facility or other material committed sources of capital. To the extent operating and capital resources are insufficient to meet future requirements, we will have to raise additional funds to continue the development and commercialization of our technologies and products. Such funds may not be available on favorable terms, or at all. In particular, our substantial leverage may limit our ability to obtain additional financing. In addition, as an early stage biotechnology company, we do not qualify to issue investment grade debt and therefore any financing we do undertake will likely involve the issuance of equity, convertible debt instruments and/or high-yield debt. These sources of capital may not be available to us in the event we require additional financing. If adequate funds are not available on reasonable terms, we may be required to curtail operations significantly or obtain funds by entering into financing, supply or collaboration agreements on unattractive terms. Our inability to raise capital could negatively impact our business.

If we fail to manage our growth effectively, our business may suffer.

Our ability to offer commercially viable products, achieve our expansion objectives, manage our growth effectively and satisfy our commitments under our collaboration agreements depends on a variety of factors, all of which must be successfully managed. Key factors include our ability to develop products internally, enter into

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strategic partnerships with collaborators, attract and retain skilled employees and effectively expand our internal organization to accommodate anticipated growth including integration of any potential businesses that we may acquire. If we are unable to manage some or all of these factors effectively, our business could grow too slowly or too quickly to be successfully sustained, thereby resulting in material adverse effects on our business, financial condition and results of operations.

If we acquire additional companies, products or technologies, we may not be able to effectively integrate personnel and operations and such failure may disrupt our business and results of operations.

We have acquired companies, products and/or technologies in the past, and may continue to acquire or make investments in complementary companies, products or technologies in the future. We may not receive the anticipated benefits of these acquisitions or investments. We may face risks relating to difficult integrations of personnel, technology and operations, uncertainty whether any integration will be successful and whether earnings will be negatively affected, and potential distractions to our management with respect to these acquisitions. In addition, our earnings may suffer because of acquisition-related costs.

We expect to continue to lose money for the next few years and may not reach profitability if our products do not generate sufficient revenue.

We have never had a profitable year and, through December 31, 2004, we have an accumulated deficit of approximately $717.1 million. We expect to continue to incur substantial and potentially increasing losses over at least the next few years as we expand our research and development efforts, testing activities and manufacturing operations, and as we further expand our late stage clinical and early commercial production facilities. Most of our potential products are in the early stages of development. Except for the approved products incorporating our Advanced PEGylation Technology, we have generated no revenues from product sales. Our revenues to date have consisted primarily of payments under short-term research and feasibility agreements and development contracts.

To achieve and sustain profitable operations, we must, alone or with others, successfully develop, obtain regulatory approval for, manufacture, introduce, market and sell products using our drug delivery technologies. There is risk that we will not generate sufficient product or contract research revenue to become profitable or to sustain profitability.

Anti-takeover provisions in our charter documents and under Delaware law may make it more difficult to acquire us, even though such acquisitions may be beneficial to our stockholders.

Provisions of our certificate of incorporation and bylaws, as well as provisions of Delaware law, could make it more difficult for a third party to acquire us, even though such acquisitions may be beneficial to our stockholders. These anti-takeover provisions include:

- establishment of a classified board of directors such that not all members of the board may be elected at one time;
- lack of a provision for cumulative voting in the election of directors, which would otherwise allow less than a majority of stockholders to elect director candidates;

the ability of our board to authorize the issuance of blank check preferred stock to increase the number of outstanding shares and thwart a takeover attempt;

prohibition on stockholder action by written consent, thereby requiring all stockholder actions to be taken at a meeting of stockholders;

establishment of advance notice requirements for nominations for election to the board of directors or for proposing matters that can be acted upon by stockholders at stockholder meetings; and

limitations on who may call a special meeting of stockholders.

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Further, we have in place a preferred share purchase rights plan, commonly known as a poison pill. The provisions described above, our poison pill and provisions of Delaware law relating to business combinations with interested stockholders may discourage, delay or prevent a third party from acquiring us. These provisions may also discourage, delay or prevent a third party from acquiring a large portion of our securities, or initiating a tender offer or proxy contest, even if our stockholders might receive a premium for their shares in the acquisition over the then current market prices.

We expect our stock price to remain volatile.

Our stock price is volatile. In the twelve-month period ending December 31, 2004, based on closing bid prices on The NASDAQ National Market, our stock price ranged from $9.69 to $23.24. We expect our stock price to remain volatile. A variety of factors may have a significant effect on the market price of our common stock, including:

- clinical trial results or product development delays or delays in product approval or launch;
- announcements by collaboration partners as to their plan or expectations related to products using our technologies;
- announcement or termination of collaborative relationships by us or our competitors;
- fluctuations in our operating results;
- developments in patent or other proprietary rights;
- announcements of technological innovations or new therapeutic products;
- governmental regulation;
- public concern as to the safety of drug formulations developed by us or others; and
- general market conditions.

Any litigation brought against us as a result of this volatility could result in substantial costs and a diversion of our management s attention and resources, which could negatively impact our financial condition, revenues, results of operations, and the price of our common stock.

New and potential new accounting pronouncements may impact our future financial position and results of operations.

There may be potential new accounting pronouncements or regulatory rulings, which may have an impact on our future financial position and results of operations. For example, in December 2004, the FASB issued an amendment to SFAS No. 123, *Accounting For Stock-Based Compensation (FAS 123R)*, which becomes effective for public companies in periods beginning after June 15, 2005. We will be required to implement the proposed standard no later than the quarter that begins July 1, 2005. The cumulative effect of adoption, if any, applied on a modified prospective basis, would be measured and recognized on July 1, 2005. SFAS No. 123 would eliminate the ability to account for share-based compensation transactions using Accounting Principles Board Opinion No. 25 (APB 25), and would instead require companies to recognize compensation expense using a fair-value based method for costs related to share-based payments including stock options and employee stock purchase plans. The adoption of SFAS No. 123R will materially impact our financial position and results of operations.

Our business is subject to changing regulation of corporate governance and public disclosure that has increased both our costs and the risk of noncompliance.

We are subject to rules and regulations of federal, state and financial market exchange entities charged with the protection of investors and the oversight of companies whose securities are publicly traded. These entities,

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including the Public Company Accounting Oversight Board, the SEC and NASDAQ, have recently issued new requirements and regulations and continue to develop additional regulations and requirements in response to recent laws enacted by Congress, most notably The Sarbanes-Oxley Act of 2002 (SOX). Our efforts to comply with these new regulations have resulted in, and are likely to continue to result in, increased general and administrative expenses and a diversion of management time and attention to SOX compliance activities.

In particular, our efforts to comply with Section 404 of SOX and the related regulations regarding our required assessment of our internal controls over financial reporting and our external auditors audit of that assessment has required, and continues to require, the commitment of significant financial and managerial resources. Our management has determined, as of the year ended December 31, 2004, that we had a material weakness in our internal control over financial reporting and that our disclosure controls and procedures were not effective. Efforts to remedy these deficiencies may require significant additional financial and managerial resources. In addition, such deficiencies may result in a loss of investor confidence and may adversely affect the price of our common stock.

Moreover, because these laws, regulations, and standards are subject to varying interpretations, their application in practice may evolve over time as new guidance becomes available. This evolution may result in continuing uncertainty regarding compliance matters and additional costs necessitated by ongoing revisions to our disclosure and governance practices. The continuing uncertainty that we will meet or continue to meet the requirements of these laws, regulations, and standards, may negatively impact our business operations and financial position.

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EXECUTIVE OFFICERS OF THE REGISTRANT

The following table sets forth the names, ages and positions of our executive officers as of February 28, 2005:

Name	Age	Position
Robert B. Chess	48	Executive Chairman of the Board
Ajit S. Gill	56	Director, Chief Executive Officer, and President
Ajay Bansal	43	Vice President, Finance and Administration, Chief Financial Officer
John S. Patton, Ph.D.	58	Director, Founder, and Chief Scientific Officer
David Johnston, Ph.D.	54	Senior Vice President, Research and Development
Nevan C. Elam	37	General Counsel and Secretary

Robert B. Chess, has served as Executive Chairman of our board since April 1999, and as a director since May 1992. Mr. Chess served as Co-Chief Executive Officer from August 1998 to April 2000, as President from December 1991 to August 1998, and as Chief Executive Officer from May 1992 to August 1998. From September 1990 until October 1991, he was an Associate Deputy Director in the White House Office of Policy Development. In March 1987, Mr. Chess co-founded Penederm Incorporated, a topical dermatological drug delivery company, and served as its President until February 1989. Prior to co-founding Penederm, Mr. Chess held management positions at Intel Corp., a semiconductor manufacturer, and Metaphor, a computer software company (acquired by International Business Machines Corp.). Mr. Chess holds a B.S. in Engineering from the California Institute of Technology and an M.B.A. from the Harvard Business School. Mr. Chess is a director of Pharsight Corp., a software company, the Biotechnology Industry Organization, a trade organization serving and representing the emerging biotechnology industry and CoTherix, Inc., a cardiopulmonary therapeutics company.

Ajit S. Gill has served as our Chief Executive Officer since April 2000, as President since April 1999, and as a director since April 1998. From August 1998 to April 2000, Mr. Gill served as our Co-Chief Executive Officer. From October 1996 to August 1998, Mr. Gill served as our Chief Operating Officer and directed our Technical Operations organization, including research and development. From January 1993 to October 1996, Mr. Gill served as our Chief Financial Officer. Before joining us, Mr. Gill was Vice President and General Manager of Kodak s Interactive Systems Products Division. Mr. Gill has served as Vice President, Finance and Chief Financial Officer for TRW-Fujitsu and Director of Business Development for VisiCorp, a pioneer in the personal computer software market. He holds a Bachelor of Technology from the Indian Institute of Technology, an M.S. in Electrical Engineering from the University of Nebraska, and an M.B.A. from the University of Western Ontario.

Ajay Bansal has served as our Vice President of Finance and Administration and Chief Financial Officer since February 2003. From July 2002 until joining Nektar, Mr. Bansal served as Director of Operations Analysis at Capital One Financial. From August 1998 to June 2002, Mr. Bansal was at Mehta Partners LLC, a financial advisory firm and was a Partner there since January 2000. Prior to joining Mehta Partners LLC, Mr. Bansal spent more than 10 years in management roles at Novartis, a major pharmaceutical company, and in consulting at Arthur D. Little, Inc., McKinsey & Company, Inc. and ZS Associates. Mr. Bansal holds a Bachelor of Technology from the Indian Institute of Technology, an M.S. in Operations Management from Northwestern University and an M.B.A. from Northwestern University.

John S. Patton, Ph.D., our co-founder, has served as Chief Scientific Officer since November 2001 and as a director since July 1990. Dr. Patton served as Vice President, Research from December 1991 to November 2001. He served as our President from incorporation in July 1990 to December 1991. From 1985 to 1990, Dr. Patton was a Project Team Leader with Genentech, Inc., a biotechnology company, where he headed their non-invasive drug delivery activities. Dr. Patton was on the faculty of the Marine Science and Microbiology Departments at the University of Georgia from 1979 through 1985, where he was granted tenure in 1984. Dr. Patton received a B.S. in Zoology and Biochemistry from Pennsylvania State University, an M.S. from the University of Rhode Island, a Ph.D. in Biology from the University of California, San Diego

and received post doctorate fellowships

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from Harvard Medical School and the University of Lund, Sweden, both in biomedicine. Dr. Patton is also a director of Saegis Pharmaceuticals, Inc., and Halozyme Therapeutics, Inc., both biopharmaceutical companies.

David Johnston, Ph.D. joined Nektar in January 2004 as Senior Vice President of Research and Development. Dr. Johnston has more than 25 years of broad experience in the international pharmaceutical industry. Prior to Nektar, he was vice president and chief development officer at Control Delivery Systems Inc., a company engaged in improving traditional treatments with innovative approaches to drug delivery. Previously, he was the executive vice president and president of AAI International (now AAI Development Services), a leading company in contract pharmaceutical R&D. He was also executive vice president of drug development and chief scientific officer of Oread Inc. From 1979 to 1997, Dr. Johnston held various positions in pharmaceutical development at Sterling Winthrop/Sanofi Winthrop Inc. In his last position at Sanofi research, he was the vice president of pharmaceutical product development for Sanofi R&D in the USA and deputy group director of product development worldwide. Dr Johnston received a B.Sc. in Chemistry (1st class) and a Ph.D. from St. Andrews University, Scotland, and he completed postdoctoral studies at the Max Planck Institute for Medicinal research in Heidelberg, Germany. He has over 40 publications and has contributed to presentations in Europe and the U.S.

Nevan C. Elam has served as General Counsel and Secretary since January 17, 2005. From March 2004 to December 2004, Mr. Elam served as an advisor to E2open, Inc., a supply chain software company. From February 2002 to March 2004, Mr. Elam served as Chief Financial Officer of E2open and from October 2000 to February 2002, he was Vice President Business and Corporate Development and General Counsel of E2open. Prior to his management roles at E2open, Mr. Elam was a Partner in the corporate practice of the law firm of Wilson Sonsini Goodrich & Rosati, where he worked for eight years. Mr. Elam received his Juris Doctorate from Harvard Law School and a Bachelor of Arts from Howard University.

Item 2. Properties

We currently lease facilities in San Carlos, California and a complex in Bradford, England. We own two facilities in Huntsville, Alabama.

We currently occupy a facility in San Carlos that covers approximately 230,000 square feet and is leased pursuant to a 15-year lease agreement expiring in June 2012. This facility serves as our corporate headquarters and is used for research and development, manufacturing and administration. This manufacturing facility operates under cGMP and has been approved and licensed by the State of California to manufacture clinical supplies for use in human clinical trials.

We also occupy a second facility in San Carlos that covers approximately 215,600 square feet. The lease on an approximate 45,600 square feet expires in August 2007, while the lease on the remaining approximate 170,000 square feet expires in September 2016. This facility houses research and development and administrative offices.

We have two locations in Huntsville, Alabama related to our Advanced PEGylation Technology operations which we own. Our Church Street location is the site for the manufacture of PEG derivatives and is approximately 85,000 square feet and is owned by us. Our Discovery Drive location is approximately 50,000 square feet and is owned by us. This facility houses research and development and administrative offices.

We currently occupy a complex in Bradford, England that covers approximately 17,500 square feet, consisting of several units with varying lease terms through 2009. This facility is used for research and development, clinical research and administration related to our supercritical

fluids technology.

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Item 3. Legal Proceedings

On September 3, 2004, a purported securities class action complaint styled Norman Rhodes, et al. v. Nektar Therapeutics, Ajit Gill, J. Milton Harris, and Robert B Chess, Case No. C 04-03735 JSW, was filed in the United States District Court for the Northern District of California against Nektar Therapeutics (the Company) and certain of its current officers and directors. The complaint alleges violations of Sections 10(b) and 20(a) of the Securities Exchange Act of 1934, and Rule 10b-5. The plaintiff seeks to represent a putative class of all purchasers of the Company s securities between March 4, 2004 and August 4, 2004 (the Class Period). The complaint generally alleges that, during that Class Period, the Company and the individual defendants made false or misleading statements in certain press releases regarding Exubera®. The Complaint seeks unspecified monetary damages and other relief against all defendants. One motion for appointment of a lead plaintiff has been filed, and that motion is pending. The action is in a very early stage, and defendants have not responded to the complaint.

This litigation may be costly and could prove to be time consuming and disruptive to normal business operations. There can be no assurance that we will prevail or that the cost of defending these lawsuits will be covered by our insurance policies. While it is not possible to predict accurately or to determine the eventual outcome of this litigation, an unfavorable outcome or settlement of this litigation could have a material adverse effect on our financial position, liquidity or results of operations.

From time to time, we may be involved in lawsuits, claims, investigations and proceedings, consisting of intellectual property, commercial, employment and other matters, which arise in the ordinary course of business. In accordance with SFAS No. 5, *Accounting for Contingencies*, we make a provision for a liability when it is both probable that a liability has been incurred and the amount of the loss can be reasonably estimated. These provisions are reviewed at least quarterly and adjusted to reflect the impact of negotiations, settlements, rulings, advice of legal counsel, and other information and events pertaining to a particular case. Litigation is inherently unpredictable. If any unfavorable ruling were to occur in any specific period, there exists the possibility of a material adverse impact on the results of operations of that period on our cash and/or liquidity.

Item 4. Submission of Matters to a Vote of Security Holders

No matters were submitted to a vote of our security holders in the three-month period ended December 31, 2004.

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PART II

Item 5. Market for Registrant s Common Stock and Related Stockholder Matters

Our Common Stock trades on the NASDAQ National Market under the symbol NKTR. The table below sets forth the high and low closing sales prices for our Common Stock (as reported on the NASDAQ National Market) during the periods indicated.

	High	Low
Year Ended December 31, 2003:		
1st Quarter	$ 9.21	$ 4.46
2nd Quarter	13.44	6.35
3rd Quarter	14.06	6.87
4th Quarter	14.94	12.65
Year Ended December 31, 2004:		
1st Quarter	$ 23.24	$ 14.30
2nd Quarter	22.83	16.33
3rd Quarter	19.81	9.69
4th Quarter	20.46	13.95

As of February 28, 2005, there were approximately 365 holders of record of our Common Stock. We have not paid any cash dividends since our inception and do not intend to pay any cash dividends in the foreseeable future.

Information regarding our equity compensation plans as of December 31, 2004 is disclosed in Item 12, Security Ownership of Certain Beneficial Owners and Management and Related Stockholders Matters and incorporated by reference from the definitive proxy statement for our 2005 Annual Meeting of Stockholders to be filed with the SEC pursuant to Regulation 14A not later than 120 days after the end of the fiscal year covered by this Form under the heading Equity Compensation Plan Information.

Sales of Unregistered Securities

In April 2004, we called for redemption of all of our outstanding 6 3/4% convertible subordinated notes due October 2006. Holders of all but $10,000 in principal amount converted their notes prior to the redemption date, resulting in the issuance of approximately 0.5 million shares of our common stock. We redeemed the $10,000 in principal amount not converted into equity for cash in the amount of $10,000. The aggregate amount of notes converted was approximately $7.8 million.

In March 2004, we called for the full redemption of our outstanding 3% convertible subordinated notes due June 2010. The aggregate principal amount outstanding of the notes at the time of the call for redemption was $133.3 million, all of which was converted into approximately 11.7 million shares of common stock prior to the redemption date. In connection with the conversion, we agreed to pay $75.00 per $1,000 of the notes to be converted, for an aggregate payment of approximately $10.0 million. This payment was recorded as interest expense.

In February 2004, certain holders of our outstanding 3% convertible subordinated notes due June 2010 converted approximately $36.0 million in aggregate principal amount of such notes for approximately 3.2 million shares of our common stock and a cash payment of approximately $3.1 million in the aggregate in privately negotiated transactions.

In January 2004, certain holders of our outstanding 3.5% convertible subordinated notes due October 2007 completed an exchange and cancellation of $9.0 million in aggregate principal amount of the notes for the issuance of approximately 0.6 million shares of our common stock in a privately negotiated transaction.

These issuances of unregistered securities were exempt from registration pursuant to Section 3(a)(9) of the Securities Act of 1933, as amended.

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Item 6. Selected Consolidated Financial Data

SELECTED CONSOLIDATED FINANCIAL INFORMATION

(In thousands, except per share information)

The selected consolidated financial data set forth below should be read together with the consolidated financial statements and related notes, Management s Discussion and Analysis of Financial Condition and Results of Operations, and the other information contained herein.

	Years Ended December 31,				
	2004	2003	2002	2001	2000
Statement of Operations Data:					
Revenue:					
Contract research revenue	$ 89,185	$ 78,962	$ 76,380	$ 68,899	$ 51,629
Product sales	25,085	27,295	18,465	8,569	
Total revenue	114,270	106,257	94,845	77,468	51,629
Total operating costs and expenses (1)	188,212	171,012	193,658	333,213	116,652
Loss from operations (1) (3)	(73,942)	(64,755)	(98,813)	(255,745)	(65,023)
Gain (Loss) on debt extinguishment	(9,258)	12,018			
Debt conversion premium, net					(40,687)
Interest and other income (expense), net (1)	(18,849)	(12,984)	(8,655)	5,737	8,307
Benefit (provision) for income taxes	163	(169)			
Net loss	$ (101,886)	$ (65,890)	$ (107,468)	$ (250,008)	$ (97,403)
Basic and diluted net loss per share	$ (1.30)	$ (1.18)	$ (1.94)	$ (4.71)	$ (2.32)
Shares used in computation of basic and diluted net loss per share (2)	78,461	55,821	55,282	53,136	41,998

	Years Ended December 31,				
	2004	2003	2002	2001	2000
Balance Sheet Data:					
Cash, cash equivalents and short-term investments	$ 418,740	$ 285,967	$ 293,969	$ 344,356	$ 484,841
Working capital	398,886	259,641	247,324	301,642	462,840
Total assets	744,921	616,788	606,638	667,241	629,540
Long-term debt (excluding current portion)	45,860	43,642	35,021	37,130	20,118
Convertible subordinated notes and debentures	173,949	359,988	299,149	299,149	299,149
Accumulated deficit	(717,121)	(615,235)	(549,345)	(441,877)	(191,869)
Total stockholders equity	467,342	164,191	206,770	270,313	277,833

Note: Amounts for the year ended December 31, 2000 do not include the operations of our Nektar, UK subsidiary which was acquired in January 2001, and our Nektar, AL subsidiary which was acquired in June 2001.

(1) Certain prior year amounts reported in our Annual Report on Form 10-K for the year ended December 31, 2003, as amended, have been restated to correct for certain misapplications of GAAP. Refer to Item 7, Management s Discussion and Analysis of Financial Condition and Results of Operations and note 1 of our consolidated financial statements in Item 8 of this Annual Report on Form 10-K/A, Amendment No. 1.

(2) Basic and diluted net loss per share is based upon the weighted average number of common shares outstanding. The shares shown above retroactively reflect a two-for-one split, effective August 22, 2000.

(3) We changed our method of accounting for goodwill and other intangible assets on January 1, 2002 in connection with the adoption of SFAS No. 142, *Goodwill and Other Intangible Assets.*

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Item 7. Management s Discussion and Analysis of Financial Condition and Results of Operations

The following discussion contains forward-looking statements that involve risks and uncertainties. Our actual results could differ materially from those discussed here. Factors that could cause or contribute to such differences include, but are not limited to, those discussed in this section as well as in Part I of this report under the heading Risk Factors.

Overview

Our business is to create high value products through the application of advanced drug delivery. We have three drug delivery technology platforms that are designed to improve the performance of molecules. These platforms are: Nektar Advanced PEGylation Technology, Nektar Pulmonary Technology and Nektar Supercritical Fluid (SCF) Technology.

Our mission is to develop superior therapeutics to make a difference in patients lives. We pursue our mission in two ways. First, we partner with pharmaceutical and biotechnology companies that seek to improve and differentiate their products. In addition, we are in the early-stages of development of our own proprietary products. We are working to become one of the world s leading drug delivery products companies.

To date the revenues we have received from the sales of our products and in connection with our collaborative arrangements have been insufficient to meet our operating and other expenses. Except for sales from certain products using Nektar Advanced PEGylation Technology, we have not sold any commercial products and do not anticipate receiving significant revenue from product sales or royalties in the near future. The development of a successful product is dependent upon several factors that are outside of our control. These include, among other things, the need to obtain regulatory approval to market these products and our dependence upon our collaborative partners. As a result of these or other risks, potential products for which we have invested substantial amounts in research and development may never produce revenues or income.

We have generally been compensated for research and development expenses during initial feasibility work performed under collaborative arrangements for all three of our technologies: Nektar Advanced PEGylation Technology, Nektar Pulmonary Technology, and Nektar Supercritical Fluid Technology. Prior to commercialization of pulmonary delivery and Advanced PEGylation products, we receive revenues from our partners for partial or full funding of research and development activities and progress payments upon achievement of certain developmental milestones. In a typical Advanced PEGylation Technology collaboration, we manufacture and supply the polyethylene glycol (PEG) reagents and receive manufacturing revenues and possible royalties from sales of the commercial product. In a typical Pulmonary Technology collaboration, our partner will provide the active pharmaceutical ingredient (the majority of which are already approved by the FDA in another delivery form), fund clinical and formulation development, obtain regulatory approvals, and market the resulting commercial product. We may manufacture and supply the drug delivery approach or drug formulation, and may receive revenues from drug manufacturing, as well as royalties from sales of most commercial products. In addition, for products using our Pulmonary Technology, we may receive revenues from the supply of our device for the product along with revenues for any applicable drug processing or filling. In addition to our partner-funded programs, we are applying our technologies independently through internal proprietary product development efforts. To achieve and sustain profitable operations, we, alone or with others, must successfully develop, obtain regulatory approval for, manufacture, introduce, market, and sell products using our drug delivery and other drug delivery systems. There can be no assurance that we can generate sufficient product or contract research revenue to become profitable or to sustain profitability.

To fund the substantial expense related to our research and development activities, we have raised significant amounts of capital through the sale of our equity and convertible debt securities. As of December 31, 2004, we had approximately $173.9 million in long-term convertible subordinated notes and debentures, $23.6 million in non-current capital lease obligations, and $22.3 million in other long-term debt. Our ability

to meet the repayment obligations of this debt is dependent upon our ability to develop successful products without significant delay or expense. Even if we are successful in this regard, we will likely require additional capital to repay our debt obligations.

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We do not expect that sales of our currently marketed products will be sufficient for us to achieve profitability. Our ability to achieve profitability is dependent on the approval of and successful marketing of products with significant markets, and for which we realize relatively higher royalties.

Recent Developments

In March 2005, we reported that Pfizer Inc and The Sanofi-Aventis Group announced that the United States Food and Drug Administration (FDA) had accepted for filing a new drug application for Exubera® (inhaled insulin). Pfizer Inc and Sanofi-Aventis stated that they intended to seek approval to market Exubera® for adult patients with type 1 and type 2 diabetes and they also stated that Exubera® has been studied in more than 3,500 patients, and in some of these patients for more than seven years.

In December, 2004, we reported that Eyetech Pharmaceuticals, Inc. and Pfizer Inc. announced that FDA had approved Macugen® (pegaptanib sodium injection) for use in the treatment of neovascular (wet) age-related macular degeneration (AMD), an eye disease associated with aging that destroys central vision. This is the sixth product using our Advanced PEGylation Technology approved for use in the U.S.

In September 2004, Pfizer and Sanofi-Aventis presented new data from a trial whose primary objective was to assess long-term pulmonary safety that showed that Exubera® was effective and well tolerated in controlling blood glucose levels over a two-year period in patients with type 2 diabetes.

During 2004 and January 2005, we announced five new collaborative agreements with Pfizer, GlaxoSmithKline, Bayer, Zelos, and one undisclosed biotechnology company.

We currently have four development programs underway through our Proprietary Products Group, including one product that has entered a Phase I clinical trial, one that has entered proof-of-concept clinical testing, and two in pre-clinical testing.

Recent Accounting Pronouncements

In December 2004, the Financial Accounting Standards Board (FASB) released a revision to Statement of Financial Accounting Standard (SFAS) No. 123, *Accounting for Stock-Based Compensation* (FAS 123R). FAS 123R addresses the accounting for share-based payment transactions in which an enterprise receives employee services in exchange for (a) equity instruments of the enterprise or (b) liabilities that are based on the fair value of the enterprise s equity instruments or that may be settled by the issuance of such equity instruments. The statement would eliminate the ability to account for share-based compensation transactions using APB Opinion No. 25, Accounting for Stock Issued to Employees, and generally would require instead that such transactions be accounted for using a fair-value-based method. We will be required to adopt FAS 123R on July 1, 2005. When we adopt the new statement, we will have to recognize substantially more compensation expense. This will have a material adverse impact on our financial position and results of operations. We are currently in the process of evaluating the effect of adopting FAS 123R.

In December 2004, the FASB issued SFAS No. 153, *Exchanges of Nonmonetary Assets,* an amendment of APB Opinion No. 29. Statement 153 addresses the measurement of exchanges of nonmonetary assets and redefines the scope of transactions that should be measured based on the fair value of the assets exchanged. SFAS No. 153 is effective for nonmonetary asset exchanges beginning July 1, 2005. We do not believe adoption of SFAS No. 153 will have a material effect on our consolidated financial position, results of operations or cash flows.

In December 2004, the FASB issued FASB Staff Position No. FAS 109-1, *Application of FASB Statement No. 109, Accounting for Income Taxes, to the Tax Deduction on Qualified Production Activities Provided by the American Jobs Creation Act of 2004*. Also in December 2004, the FASB issued FASB Staff Position No. FAS 109-2, *Accounting and Disclosure Guidance for the Foreign Earnings Repatriation Provision within the*

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American Jobs Creations Act of 2004. We do not expect the adoption of these new tax accounting standards to have a material impact on our consolidated financial position, results of operations, or cash flows.

In November 2004, the FASB released SFAS No. 151, *Inventory Costs An Amendment to ARB No. 43.* This Statement amends the guidance in ARB No. 43, Chapter 4, Inventory Pricing, to clarify the accounting for abnormal amounts of idle facility expense, freight, handling costs, and wasted material. This Statement requires that those items be recognized as current-period charges regardless of whether they meet the criterion of so abnormal as defined by ARB No. 43, Chapter 4, *Inventory Pricing*. In addition, this Statement requires that allocation of fixed production overheads to the costs of conversion be based on the normal capacity of the production facilities. We will be required to adopt SFAS No. 151 on January 1, 2006. We are currently in the process of evaluating the effect of adopting SFAS No. 151.

In June 2004, the FASB Emerging Issues Task Force (EITF) issued EITF 02-14, *Whether an Investor Should Apply the Equity Method of Accounting to Investments Other Than Common Stock*. EITF 02-14 addresses whether the equity method of accounting applies when an investor does not have an investment in voting common stock of an investee but exercises significant influence through other means. The accounting provisions of EITF 02-14 are effective for reporting periods beginning after September 15, 2004. We do not expect the adoption of EITF 02-14 to have a material impact on our consolidated financials position, results of operations, or cash flows.

In March 2004, the EITF reached a consensus on EITF 03-01, *The Meaning of Other-Than-Temporary Impairment and Its Application to Certain Investments*. EITF 03-01 provides guidance regarding disclosures about unrealized losses on available-for-sale debt and equity securities accounted for under SFAS No. 115, *Accounting for Certain Investments in Debt and Equity Securities.* In September 2004, the EITF delayed the effective date for the measurement and recognition guidance; however the disclosure requirements remain effective for annual periods ending after June 15, 2004 (see note 2). We have complied with the disclosure requirements of EITF 03-01, and we will evaluate the impact of the measurement and recognition provisions of EITF 03-01 once final guidance is issued.

Critical Accounting Estimates

Our discussion and analysis of our financial condition and results of operations are based on our consolidated financial statements, which have been prepared in conformity with accounting principles generally accepted in the United States. It requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the reporting period. Actual results could differ from those estimates. Management has discussed the development, selection, and disclosure of each of the following critical accounting estimates with the audit committee.

Stock Based Compensation

In December 2004, the Financial Accounting Standards Board released a revision to SFAS No. 123, *Accounting for Stock-Based Compensation* (FAS 123R). FAS 123R addresses the accounting for share-based payment transactions in which an enterprise receives employee services in exchange for (a) equity instruments of the enterprise or (b) liabilities that are based on the fair value of the enterprise s equity instruments or that may be settled by the issuance of such equity instruments. The statement would eliminate the ability to account for share-based compensation transactions using APB Opinion No. 25, Accounting for Stock Issued to Employees, and generally would require instead that such transactions be accounted for using a fair-value-based method. We will be required to adopt FAS 123R on July 1, 2005. When we adopt the new statement, we will have to recognize substantially more compensation expense. This would have a material adverse impact on our financial position and results of operations. We are currently in the process of evaluating the effect of adopting FAS 123R.

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We currently apply the recognition and measurement principles of APB Opinion No. 25, *Accounting for Stock Issued to Employees*, and related interpretations in accounting for those plans. Under this opinion, no stock-based employee compensation expense is charged for options that were granted at an exercise price that was equal to the market value of the underlying common stock on the date of grant. Stock compensation costs are immediately recognized to the extent the exercise price is below the fair value on the date of grant and no future vesting criteria exist.

For stock awards issued below our market price on the date of grant, we record deferred compensation representing the difference between the price per share of stock award issued and the fair value of the Company s common stock at the time of issuance or grant, and we amortize this amount over the related vesting periods on a straight-line basis.

Pro forma information regarding net income and earnings per share required by SFAS 123, as amended by SFAS 148, regarding the fair value for employee options and employee stock purchase plan shares was estimated at the date of grant using a Black-Scholes option valuation model with the following weighted-average assumptions:

	2004	2003	2002
Risk-free interest rate	3.3%	2.8%	3.8%
Dividend yield	0.0%	0.0%	0.0%
Volatility Factor	0.707	0.744	0.743
Weighted average expected life	5 years	5 years	5 years

The Black-Scholes options valuation model was developed for use in estimating the fair value of traded options, which have no vesting restrictions and are fully transferable. In addition, option valuation models require the input of highly subjective assumptions including the expected stock price volatility. We have presented the pro forma net loss and pro forma basic and diluted net loss per common share using the assumptions noted above.

The following table illustrates the effect on net income and earnings per share if we had applied the fair value recognition provisions of SFAS 123 to stock-based employee compensation (in thousands, except per share information):

	Years Ended December 31,		
	2004	2003	2002
Net loss, as reported	$ (101,886)	$ (65,890)	$ (107,468)
Add: stock-based employee compensation included in reported net loss	1,423	878	644
Deduct: total stock-based employee compensation expense determined under fair value methods for all awards	(31,185)	(34,300)	(35,605)
Pro forma net loss	$ (131,648)	$ (99,312)	$ (142,429)
Net loss per share			
Basic and diluted, as reported	$ (1.30)	$ (1.18)	$ (1.94)
Basic and diluted, pro forma	$ (1.68)	$ (1.78)	$ (2.58)

Cash, Cash Equivalents and Investments

We consider all highly liquid investments with a maturity at the date of purchase of three months or less to be cash equivalents. Cash and cash equivalents include demand deposits held in banks, interest bearing money market funds, commercial paper, federal and municipal government securities, and repurchase agreements.

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Short-term investments consist of: 1) auction rate securities with varying maturities, and 2) federal and municipal government securities, corporate bonds, and commercial paper with A1, F1, or P1 short-term ratings and A or better long-term ratings with remaining maturities at date of purchase of greater than 90 days and less than two years. Investments with maturities greater than two years are classified as short-term when they represent investments of cash that are reasonably expected to be realized in cash and are available for use in current operations.

At December 31, 2004, all short-term investments are designated as available-for-sale and are carried at fair value, with unrealized gains and losses reported in stockholders equity as accumulated other comprehensive income (loss). Short-term investments are adjusted for amortization of premiums and accretion of discounts to maturity. Such amortization is included in interest income. Realized gains and losses and declines in value judged to be other-than-temporary on available-for-sale securities, if any, are included in other income (expense). The cost of securities sold is based on the specific identification method. Interest and dividends on securities classified as available-for-sale are included in interest income.

At December 31, 2004 and 2003, we had letter of credit arrangements with certain vendors including our landlord totaling $2.2 million and $6.5 million, respectively, which are secured by investments in similar amounts.

Impairment of Goodwill, Intangible Assets, and Other Long-Lived Assets

Goodwill is tested for impairment at least annually, or on an interim basis if an event occurs or circumstances change that would more-likely-than-not reduce the fair value below our carrying value. We performed our annual impairment test and determined that on a consolidated basis, the undiscounted cash flow from our long-range forecast exceeds the carrying amount of our goodwill. The carrying value of goodwill is $130.1 million as of December 31, 2004 and 2003.

Goodwill will be tested for impairment using a two-step approach. The first step is to compare our fair value to our net asset value, including goodwill. If the fair value is greater than our net asset value, goodwill is not considered impaired and the second step is not required. If the fair value is less than our net asset value, the second step of the impairment test measures the amount of the impairment loss, if any. The second step of the impairment test is to compare the implied fair value of goodwill to its carrying amount. If the carrying amount of goodwill exceeds its implied fair value, an impairment loss is recognized equal to that excess. The implied fair value of goodwill is calculated in the same manner that goodwill is calculated in a business combination, whereby the fair value is allocated to all of the assets and liabilities (including any unrecognized intangible assets) as if they had been acquired in a business combination and the fair value was the purchase price. The excess purchase price over the amounts assigned to assets and liabilities would be the implied fair value of goodwill.

The impairment tests for goodwill are performed at the corporate entity level, which we have identified to be our only reporting unit. In the future, we may determine that impairment tests should be performed at a level below the reporting unit level, depending on whether certain criteria are met.

In accordance with SFAS No. 144 *Accounting for the Impairment or Disposal of Long-Lived Assets,* we perform a test for recoverability of our intangible and other long-lived assets whenever events or changes in circumstances indicate that the carrying value of the assets may not be recoverable. An impairment loss would be recognized only if the carrying amount of an intangible or long-lived asset exceeds the sum of the undiscounted cash flows expected to result from the use and eventual disposal of the asset. To date, there have been no events or changes in circumstances that would indicate that the carrying value of such assets may not be recoverable, and therefore we have determined that there has been no impairment on our intangible and other long-lived assets, including capitalized assets related to Exubera®.

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In assessing the recoverability of our intangibles and long-lived assets, we have concluded that there is no impairment in the carrying value of these assets as of December 31, 2004. If this assessment changes in the future, we may be required to record impairment charges for these assets. The carrying value of our purchased intangibles as of December 31, 2004 and 2003 is $6.5 million and $11.0 million, respectively. These assets are scheduled to be fully amortized by December 2006. The carrying value of our other long-lived assets as of December 31, 2004 and 2003 is $153.8 million and $156.7 million, respectively.

Judgments Impacting Fixed Asset Capitalization for Exubera®

In accordance with SFAS 2, *Accounting for Research and Development Costs*, we have expensed certain amounts paid for plant design, engineering, and validation costs for the automated assembly line equipment that will be used in connection with the manufacture of the inhaler device for Exubera® because such costs have no alternative future use. The total amount expensed was $1.7 million, $6.6 million, and $7.3 million, for the years ended December 31, 2004, 2003, and 2002, respectively. As of December 31, 2004, the capitalized net book value of the automated assembly line equipment located at our contract manufactures sites totals $25.2 million. These assets are intended to be used in connection with the manufacture of the inhaler device for Exubera®. The total amount capitalized amounted to $0.2 million, $1.4 million, and $4.6 million for the years ended December 31, 2004, 2003, and 2002, respectively. These amounts have been capitalized based upon our determination that the related assets have alternative future use and therefore have separate economic or realizable value.

Inventory Reserves

We perform quality control reviews of our raw materials and finished goods. We record inventory reserves based upon specific identification of potentially defective raw material and finished goods batches. In addition, we record an inspection reserve based on a historical estimate of finished goods that ultimately fail quality control. We generally do not maintain inventory reserves based on obsolescence or risk of competition because the shelf life of our products is long. However, if our current assumptions about demand or obsolescence were to change, additional inventory reserves may be needed, which could negatively impact our product gross margins. Our inventory reserves were $3.2 million and $1.6 million as of December 31, 2004 and 2003, respectively. This represented 23% and 16% of gross inventory as of December 31, 2004 and 2003, respectively.

Revenue Recognition

We recognize revenue in accordance with Securities and Exchange Commission Staff Accounting Bulletin No. 104, Revenue Recognition in Financial Statements (SAB 104). Effective July 1, 2003, we adopted the provisions of Emerging Issues Task Force, Issue No. 00-21, Revenue Arrangements with Multiple Deliverables on a prospective basis.

Revenue is recognized when there is persuasive evidence that an arrangement exists, delivery has occurred, the price is fixed and determinable, and collectability is reasonably assured. Allowances are established for uncollectible amounts.

We enter into collaborative research and development arrangements with pharmaceutical and biotechnology partners that may involve multiple deliverables. For multiple-deliverable arrangements entered into after July 1, 2003 judgment is required in the areas of separability of units of accounting and the fair value of individual elements. The principles and guidance outlined in EITF No. 00-21 provide a framework to (a) determine whether an arrangement involving multiple deliverables contains more than one unit of accounting, and (b) determine how the

arrangement consideration should be measured and allocated to the separate units of accounting in the arrangement. Our arrangements may contain the following elements: collaborative research, milestones, manufacturing and supply, royalties and license fees. For each separate unit of accounting we have objective and reliable evidence of fair value using available internal evidence for the undelivered item(s) and our arrangements

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generally do not contain a general right of return relative to the delivered item. In accordance with the guidance in EITF No. 00-21, the Company uses the residual method to allocate the arrangement consideration when it does not have fair value of a delivered item(s). Under the residual method, the amount of consideration allocated to the delivered item equals the total arrangement consideration less the aggregate fair value of the undelivered items.

Contract revenue from collaborative research and feasibility agreements is recorded when earned based on the performance requirements of the contract. Advance payments for research and development revenue received in excess of amounts earned are classified as deferred revenue until earned. Revenue from collaborative research and feasibility arrangements are recognized as the related costs are incurred. Amounts received under these arrangements are generally non-refundable if the research effort is unsuccessful.

Payments received for milestones achieved are deferred and recorded as revenue ratably over the next period of continued development. Management makes its best estimate of the period of time until the next milestone is reached. This estimate affects the recognition of revenue for completion of the previous milestone. The original estimate is periodically evaluated to determine if circumstances have caused the estimate to change and if so, amortization of revenue is adjusted prospectively.

Product sales are derived primarily from cost-plus manufacturing and supply contracts for our PEG Reagents with individual customers in our industry. Sales terms for specific PEG Reagents are negotiated in advance. Revenues related to our product sales are recorded in accordance with the terms of the contracts. No provisions for potential product returns have been made to date because we have not experienced any significant returns from our customers.

Restatement

Certain prior year amounts reported in our Annual Report on Form 10-K for the year ended December 31, 2003, as amended, have been restated to correct for misapplications of generally accepted accounting principles in the U.S. (GAAP). Also, certain amounts reported in our Quarterly Reports on Form 10-Q during the years 2004 and 2003 have been restated to correct for these misapplications of our accounting policies related to GAAP (refer to footnote 15 in Item 8 of this Annual Report on Form 10-K/A, Amendment No. 1). These reclassifications did not result in any change to our cash position, revenue, or net loss for the years ended December 31, 2003 and December 31, 2002 or for any quarterly period during the years ended December 31, 2004 or 2003.

The specific misapplications of GAAP that lead to this conclusion are as follows:

We have reclassified approximately $9.4 million and $9.8 million for the years ended December 31, 2003 and 2002, respectively, from research and development expenses to general and administrative expenses. This reclassification included legal expenses related to our intellectual property portfolio and a portion of finance, information systems, and human resource expenses that were not clearly related to research and development and are required to be classified outside research and development expenses under Statement Financial Accounting Standards No. 2, *Accounting for Research and Development Costs*.

We reclassified approximately $1.4 million and $1.3 million for the years ended December 31, 2003 and 2002, respectively, from general and administrative expenses to interest expense. This reclassification was made to record the amortization of debt issuance costs to interest expense as required under Accounting Principles Board No. 21, *Interest on Receivables and Payables* and EITF 86-15 *Increasing-Rate Debt*.

Reclassification

Subsequent to the filing of our Annual Report on Form 10-K, additional clarification was provided regarding the financial statement classification of auction rate securities held as investments. Pursuant to this

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guidance, auction rate securities are not to be classified as cash and cash equivalents. We invest in auction rate securities as part of our cash management strategy. These investments, which we have historically classified as cash and cash equivalents because of the short time frame between auction periods, have been reclassified as short-term investments. We have reclassified $72.4 million and $19.6 million of auction rate securities from cash equivalents to short-term investments as of December 31, 2004 and 2003. There was no impact on the Consolidated Statements of Operations or total current assets as a result of the reclassification for the years ended December 31, 2004 or 2003. The impact on the Consolidated Statements of Cash Flows was an increase of $52.7 million, $9.7 million, and $4.0 million in cash used in investing activities for the years ended December 31, 2004, 2003, and 2002, respectively. This reclassification did not result in any change to our revenue, total current assets, or net loss for the years ended December 31, 2004, 2003, or 2002 or for any quarterly period during the years ended December 31, 2004, 2003, or 2002.

Material Weakness and Remediation

In connection with management s assessment of its internal control over financial reporting as of December 31, 2004, we have concluded that we have a material weakness in our financial statement close process, including insufficient review of the following:

- the application of our accounting policies and
- disclosures in the notes to our financial statements.

This material weakness in our financial statement close process arises from staff with inadequate proficiency to apply the Company s accounting policies in accordance with U.S. generally accepted accounting principles.

This material weakness impacts our ability to report financial information in conformity with GAAP, which could affect all significant financial statement accounts and has resulted in (i) a restatement of the 2002 and 2003 consolidated financial statements to reflect reclassifications of certain amounts between research and development expense, general and administrative expense, and interest expense; (ii) a restatement of all four quarters of 2003 and the first three quarters of 2004 to reflect reclassifications of certain amounts between research and development expense, general and administrative expense, and interest expense; and (iii) the prior restatement of the 2003 consolidated financial statements to reduce the gain on debt extinguishment.

In 2004, we began implementation of new processes and controls and hired additional personnel with technical accounting expertise to improve our financial statement close process. We intend to continue to improve our financial statement close process in 2005 including the remediation of the material weakness discussed above by identifying, recruiting, and training personnel with the appropriate accounting skills. In addition, we plan to further enhance our technical accounting review process for non-routine and complex transactions by:

- identifying and defining non-routine and complex transactions on a regular basis, and
- researching, identifying, analyzing, documenting, and reviewing applicable accounting principles.

Our efforts to comply with Section 404 of SOX and the related regulations regarding our required assessment of our internal controls over financial reporting and the audit of that assessment by our registered public accounting firm has required, and continues to require, the commitment of significant financial and managerial resources. Our internal control systems are designed to provide reasonable assurance to management and our board of directors that our internal control over financial reporting is adequate, but there can be no guarantee that such controls will be effective. The continuing uncertainty that we will meet or continue to meet the requirements of these laws, regulations, and standards, may negatively impact our business operations and financial position.

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Results of Operations

Years Ended December 31, 2004, 2003 and 2002

Revenue (in thousands except percentages)

	2004	2003	2002	Increase/ (Decrease) 2004 vs 2003	Increase/ (Decrease) 2003 vs 2002	Percentage Increase/ (Decrease) 2004 vs 2003	Percentage Increase/ (Decrease) 2003 vs 2002
Contract Revenue	$ 89,185	$ 78,962	$ 76,380	$ 10,223	$ 2,582	13%	3%
Product Revenue	$ 25,085	$ 27,295	$ 18,465	$ (2,210)	$ 8,830	(8)%	48%
Total Revenue	$ 114,270	$ 106,257	$ 94,845	$ 8,013	$ 11,412	8%	12%

Total revenue was $114.3 million for the year ended December 31, 2004 compared to $106.3 million and $94.8 million for the years ended December 31, 2003 and 2002, respectively. Total revenue increased 8% in 2004 compared to 2003 and increased 12% in 2003 compared to 2002.

Contract research revenue included reimbursed research and development expenses as well as the amortization of deferred up-front signing and milestone payments received from our collaborative partners. Contract revenues are expected to fluctuate from year to year, and future contract revenue cannot be predicted accurately. The level of contract revenues depends in part upon the continuation of existing collaborations, signing of new collaborations, and achievement of milestones under current and future agreements.

Contract research revenue was $89.2 million for the year ended December 31, 2004 compared to $79.0 million and $76.4 million for the years ended December 31, 2003 and 2002, respectively. The increase in contract research revenue for the year ended December 31, 2004, as compared to the year ended December 31, 2003 was due primarily to an $8.9 million increase in contract research revenue from Pfizer related to the Exubera® collaboration and a $2.0 million payment received from Aventis-Behring related to the termination of their collaboration with us.

Product revenue was $25.1 million for the year ended December 31, 2004 compared to $27.3 million and $18.5 million for the years ended December 31, 2003 and 2002, respectively. Product sales accounted for 22% of revenues for the year ended December 31, 2004, as compared to 26% and 19% of revenues for the years ended December 31, 2003 and 2002, respectively. The decrease in product revenue for the year ended December 31, 2004 as compared to the year ended December 31, 2003 was due primarily to lower demand. This resulted in lower sales of the following commercially approved products: Neulasta®, Somavert®, and PEGASYS®. These reductions in sales volume were partially offset by an increase in revenue related to CDP 870 for Phase III clinical supplies.

The increase in contract research revenue for the year ended December 31, 2003, as compared to the year ended December 31, 2002 was due primarily to increased activities under our existing collaboration agreements with Chiron Corporation and Solvay Pharmaceuticals, Inc.

The increase in product revenue for the year ended December 31, 2003 as compared to the year ended December 31, 2002 was primarily due to higher sales of Neulasta®, Somavert®, and PEGASYS®.

Future product sales are dependent upon regulatory approval of new products for sale and adoption of current products in the market.

Pfizer represented 61% of our revenue for the year ended December 31, 2004, 61% for the year ended December 31, 2003, and 59% for the year ended December 31, 2002. No other single customer represented 10% or more of our total revenues for any of the three years ended December 31, 2004, 2003, or 2002.

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Cost of goods sold (in thousands except percentages)

2004	2003	2002	Increase/ (Decrease) 2004 vs 2003	Increase/ (Decrease) 2003 vs 2002
$19,798	$ 14,678	$ 7,020	$ 5,120	$ 7,658

Cost of goods sold for the year ended December 31, 2004 was $19.8 million resulting in a gross margin from product sales of 21%. Cost of goods sold for the year ended December 31, 2003 was $14.7 million resulting in a gross margin of 46%. Cost of goods sold for the year ended December 31, 2002 was $7.0 million resulting in a gross margin from product sales of 62%.

The decrease in product gross margin for the year ended December 31, 2004 compared to December 31, 2003 was primarily due to the following:

Production problems encountered during the second and third quarter of 2004 resulted in a temporary shut down of part of our manufacturing operations. This resulted in lower overhead absorption. The excess overhead not absorbed was expensed to cost of goods sold. As of December 31, 2004, we are confident that the manufacturing problems are being satisfactorily addressed.

As of January 1, 2004, we refined our methodology to allocate additional operating expenses which resulted in more overhead being allocated to production.

Inventory reserves increased $1.6 million during the year ended December 31, 2004 from $1.6 million at December 31, 2003 to $3.2 million at December 31, 2004. The reserve represented 23% and 16% of gross inventory as of December 31, 2004 and 2003, respectively. This increase in the percentage of inventory reserved was due to a larger general reserve for defective batches.

The decrease in product gross margin for the year ended December 31, 2003 compared to December 31, 2002 was primarily due to changes in product mix and an increase to inventory reserves of from $0.4 million to $1.6 million. The increase was due to the establishment of a reserve for specifically identified failed batches.

Research and development (in thousands except percentages)

2004	2003 (restated)	2002 (restated)	Increase/ (Decrease) 2004 vs 2003	Increase/ (Decrease) 2003 vs 2002	Percentage Increase/ (Decrease) 2004 vs 2003	Percentage Increase/ (Decrease) 2003 vs 2002
$133,523	$ 122,149	$ 147,627	$ 11,374	$ (25,478)	9%	(17)%

We expense all research and development costs as they are incurred. Research and development expenses were $133.5 million for the year ended December 31, 2004, as compared to $122.1 million and $147.6 million for the years ended December 31, 2003 and 2002, respectively. The 9% increase in research and development expense for the year ended December 31, 2004 as compared to the year ended December 31, 2003 was primarily attributable to increased spending relating to commercial readiness of Exubera® as well as increased internally funded development spending.

We expect research and development spending to increase over the next few years as we continue to fund development of our technologies, and because of increased spending associated with the development of internally funded proprietary products. While we believe our proprietary products strategy may result in improved economics for any products ultimately developed and approved, it will require us to invest significant funds in developing these products without reimbursement from a collaborative partner.

The 17% decrease in research and development expense for the year ended December 31, 2003 as compared to the year ended December 31, 2002 was primarily attributable a deferral of certain research and development efforts into fiscal year 2004, as well as a workforce reduction completed in December 2002.

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We have reclassified approximately $9.4 million and $9.8 million for the years ended December 31, 2003 and 2002, respectively, from research and development expenses to general and administrative expenses. This reclassification included legal expenses related to our intellectual property portfolio and a portion of finance, information systems, and human resource expenses that were not clearly related to research and development and are required to be classified outside of research and development expenses under Statement Financial Accounting Standards No. 2, *Accounting for Research and Development Costs*. The reclassification did not result in any change to our cash position, total operating expenses, or results of operations for the years ended December 31, 2003 or 2002.

The following table summarizes our partner development programs for products approved for use and those in clinical trials. The table includes the primary indication for the particular drug or product, the identity of a respective corporate partner if it has been disclosed, and the present stage of clinical development or approval in the United States, unless otherwise noted.

Molecule	Primary Indication	Partner	Status(1)
Neulasta® (pegfilgrastim)	Neutropenia	Amgen Inc.	Approved
PEGASYS® (peginterferon alfa-2a)	Hepatitis-C	Hoffmann La-Roche Ltd.	Approved
Somavert® (pegvisomant)	Acromegaly	Pfizer Inc.	Approved
PEG-INTRON® (peginterferon alfa-2b)	Hepatitis-C	Schering-Plough Corporation	Approved
Definity® (PEG)	Cardiac imaging	Bristol-Myers Squibb Company	Approved
Macugen® (pegaptanib sodium injection)	Age-related macular degeneration	Eyetech Pharmaceuticals, Inc.	Approved in the US & Filed in the EU & Canada
Macugen® (pegaptanib sodium injection)	Diabetic macular edema	Eyetech Pharmaceuticals Inc.	Phase II
Exubera® (inhaled insulin)	Diabetes	Pfizer Inc.	Filed in the U.S. and Europe
SprayGel adhesion barrier system (PEG-hydrogel)	Prevention of post-surgical adhesions	Confluent Surgical, Inc.	Pivotal trials in U.S. Approved in Europe
CDP 870 (PEG-anti-TNF alpha antibody fragment)	Rheumatoid arthritis Crohn s disease	UCB Pharma	Phase III Phase III
CERA (Continuous Erythropoiesis Receptor Activator)	Renal anemia	Hoffmann La-Roche Ltd.	Phase III
Undisclosed (PEG)	Undisclosed	Undisclosed	Phase II
CDP 791 (PEG-antibody fragment angiogenesis inhibitor)	Cancer	UCB Pharma	Phase I/II
CDP 484 (PEGylated antibody fragment targeting pro-inflammatory cytokine interleukin 1-beta)	Rheumatoid Arthritis	UCB Pharma	Phase I/II
Tobramycin inhaled powder (TIP)	Lung infection	Chiron Corporation	Phase I
Inhaled leuprolide	Endometriosis	Enzon, Inc.	Phase I
MARINOL® (inhaled dronabinol)	Multiple indications	Solvay Pharmaceuticals, Inc.	Phase I
PEGylated interferon beta	Undisclosed	Serono, Inc.	Phase I
PEG-Alfacon (PEGylated interferon alfacon-1)	Hepatitis-C	InterMune, Inc.	Phase I
PEGylated-AXOKINE	Obesity	Regeneron Pharmaceuticals	Phase I
Undisclosed (PEG)	Undisclosed	Pfizer Inc.	Phase I

(1) Status definitions are as follows:
Approved regulatory approval to market and sell product obtained in the U.S. or EU.

Phase III or Pivotal Product in large-scale clinical trials conducted to obtain regulatory approval to market and sell a drug. Typically,