NEOSE TECHNOLOGIES INC
Form 10-K
February 17, 2004
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# SECURITIES AND EXCHANGE COMMISSION

**Washington, D.C. 20549**

# FORM 10-K

**(Mark One)**

**x ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(D) OF THE SECURITIES EXCHANGE ACT OF 1934**

**For the fiscal year ended December 31, 2003**

**or**

**¨ TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(D) OF THE SECURITIES EXCHANGE ACT OF 1934**

**For the transition period from _____ to _____**

**Commission File Number 0-27718**

# NEOSE TECHNOLOGIES, INC.

**(Exact name of registrant as specified in its charter)**

| **Delaware** | **13-3549286** |
|---|---|
| **(State or other jurisdiction of incorporation or organization)** | **(I.R.S. Employer Identification No.)** |

**102 Witmer Road**

| **Horsham, Pennsylvania** | **19044** |
|---|---|
| **(Address of principal executive offices)** | **(Zip Code)** |

**Registrant s telephone number, including area code: (215) 315-9000**

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**Securities registered pursuant to Section 12(b) of the Act:**

| **None** | **None** |
|---|---|
| **(Title of each class)** | **(Name of each exchange on which registered)** |

**Securities registered pursuant to Section 12(g) of the Act:**

**Preferred Share Purchase Rights**

**(Title of class)**

**Common Stock, par value $0.01 per share**

**(Title of class)**

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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 x 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 the definitive proxy statement incorporated by reference in Part III of this Annual Report on Form 10-K or any amendment to this Annual Report on Form 10-K. ¨

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

As of June 30, 2003, the aggregate market value of the Common Stock held by non-affiliates of the registrant was approximately $88,792,350 based on the last sale price of the Common Stock on such date as reported by The Nasdaq Stock Market. This calculation excludes 8,362,360 shares held on June 30, 2003 by directors, executive officers, and two holders of more than 10% of the registrant s Common Stock.

As of February 15, 2004, there were 19,944,671 shares of the registrant s Common Stock outstanding.

**DOCUMENTS INCORPORATED BY REFERENCE**

The registrant s definitive proxy statement to be filed in connection with solicitation of proxies for its Annual Meeting of Stockholders to be held on May 6, 2004, is incorporated by reference into Part III of this Annual Report on Form 10-K.

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*NEOSE, GlycoAdvance, GlycoPEGylation and GlycoConjugation are trademarks of Neose Technologies, Inc. This Annual Report on Form 10-K also includes trademarks and trade names of other companies*

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This report includes forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. These forward-looking statements include, but are not limited to, statements about our plans, objectives, representations and contentions and are not historical facts, which typically may be identified by use of terms such as anticipate, believe, estimate, plan, may, expect, intend, cou potential, and similar expressions, although some forward-looking statements are expressed differently. You should be aware that the forward-looking statements included in this report represent management s current judgment and expectations, but our actual results, events and performance could differ materially from those in the forward-looking statements. The forward looking statements are subject to a number of risks and uncertainties which are discussed in the section of Part II entitled Factors Affecting the Company s Prospects. We do not intend to update any of these factors or to publicly announce the results of any revisions to these forward-looking statements.

## PART I

### ITEM 1. BUSINESS.

#### Overview

We are a biopharmaceutical company focused on improving protein therapeutics using our proprietary technologies. Most protein therapeutics currently on the market or in development today are glycoproteins that is, they consist of a protein backbone (comprised of amino acids) to which carbohydrate structures (chains of simple sugars) are attached. While the protein backbone determines what the protein will do, the attached carbohydrate structures known as glycosylation - are often essential to ensure its proper functioning. Inadequate glycosylation is also frequently a significant limitation to the efficiency of the manufacturing process for existing glycoprotein therapeutics.

Our core technologies, GlycoAdvance and GlycoPEGylation, enable us to manipulate, enzymatically, the carbohydrate structures of glycoproteins, and thereby pursue the objective of improving the therapeutic profiles of proteins that have already been marketed or substantially developed by other companies. We use GlycoAdvance, either to complete the carbohydrate structures on proteins that are inadequately glycosylated, or to initiate and extend the carbohydrate structures on proteins that are not glycosylated at all. As a technology, GlycoAdvance is sufficiently versatile that it enables us to work with many proteins secreted from a variety of expression systems (the basic platform for manufacturing proteins), and with proteins having various glycosylation patterns. We may also use GlycoPEGylation to attach a sugar molecule linked to polyethylene glycol (PEG) to selected carbohydrate structures. PEG is an inert polymer, which, when added to a protein, increases its size, and in most cases improves its pharmaceutical profile, such as enabling the protein to be administered less frequently.

In sum, our core business is to use our novel technologies to improve proteins for which there is already a substantial body of data demonstrating safety and efficacy. The development of next-generation products (i.e. products with improvements over the original product) has been a key strategy used by pharmaceutical and biopharmaceutical companies for decades. We intend to apply this strategy to products we are developing on our own and to products we co-develop and co-own with others, and we expect to make our technologies available, through strategic partnerships, to improve the products of other parties.

#### Opportunities in the Protein Market

Worldwide sales of protein drugs (which include monoclonal antibodies and fusion proteins) were over $39 billion in 2003, and by some estimates are expected to grow to over $70 billion by 2008. Many of the proteins now on the market will lose the protection of certain patent

claims over the next 15 years. In addition, many marketed proteins are facing increased competition from next-generation versions or from other drugs approved for the same disease indications. Although not every protein drug is a candidate for the use of our technologies, we believe our GlycoAdvance and GlycoPEGylation technologies can be applied to many of these marketed drugs to create next-generation products with improved clinical profiles. We are pursuing opportunities in this field through our own proprietary drug development program, our partnering and licensing program, and our exploratory research program.

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**Neose Proprietary Drug Program**. The initial targets of our own proprietary drug program are an improved erythropoietin (EPO) and an improved granulocyte colony stimulating factor (G-CSF). The EPO and G-CSF drug categories had combined worldwide sales of approximately $10.6 billion in 2002.

**Partnering and Licensing Program**. During 2003, we entered into two new agreements with Novo Nordisk A/S (Novo Nordisk) that allow us to partner the development and commercialization of next-generation versions of three marketed proteins, one of which is currently marketed by Novo Nordisk. These three marketed proteins had combined worldwide sales of approximately $2.0 billion in 2002.

**Exploratory Research Program**. Our exploratory research program is currently focused on the development of two undisclosed marketed proteins, one in collaboration with Rentschler Biotechnologie GmbH (Rentschler) and another with Sandoz GmbH (Sandoz). The marketed versions of these proteins had combined worldwide sales of approximately $5.5 billion in 2002.

**Core Technology**

Our GlycoAdvance and GlycoPEGylation technologies evolve from the same core the use of enzymes to modify or initiate carbohydrate structures on glycoproteins. We have developed a special expertise and strong intellectual property position in this area. Our technologies may permit the development of therapeutic proteins with improved clinical profiles. In some cases, these improvements to therapeutic proteins may also give rise to new intellectual property. We continue to make significant investments in research and development and legal services to protect and expand our intellectual property position. We believe our core technology has broad application to protein drug development and can be extended to provide an opportunity for sustainable growth.

**GlycoAdvance**. We use GlycoAdvance, either to complete the carbohydrate structures on proteins that are inadequately glycosylated, or to initiate and extend the carbohydrate structures on proteins that are not glycosylated at all. Currently, recombinant glycoprotein drugs are most often produced in mammalian cell culture expression systems, primarily Chinese hamster ovary (CHO) cells. The carbohydrates are added to these proteins during the process of expression. CHO cells, and many other expression systems used for commercial manufacturing of proteins, tend to produce protein molecules with incomplete or inconsistent carbohydrate structures. In the human body, these incompletely glycosylated proteins may be cleared too rapidly, may break down too rapidly, and may stimulate unwanted antibody responses. Conventional approaches to improving the glycosylation of recombinant protein drugs, such as changing expression cell types, re-engineering the protein, and modifying cell culture conditions or media, are time consuming and frequently provide only partial solutions. When a protein is inconsistently glycosylated, additional purification may be required to remove the incompletely glycosylated drug molecules from the desired drug product, resulting in lower manufacturing yields and increased expense.

Some proteins (e.g., human growth hormone), in their natural state, lack attached carbohydrates. Others (e.g., G-CSF) may be expressed in bacteria, an expression system that fails to add sugars at natural glycosylation sites. Using our GlycoAdvance technology, we employ enzymes to initiate glycosylation at engineered or natural acceptor sites on such proteins and to further elaborate these carbohydrate structures with natural or modified sugar units. By attaching and modifying carbohydrate structures, we have been able to demonstrate with several drug candidates a prolonged drug effect in animals. We are using GlycoAdvance in our own proprietary drug program, in our partnering and licensing program, and in our exploratory research program. We are also exploring the use of GlycoAdvance to enable alternative protein production systems, such as plants and insect cells that naturally produce only partial versions of the carbohydrate structures found in human glycoproteins.

**GlycoPEGylation**. Common protein drug delivery problems include poor solubility and stability, proteolysis (rapid degradation by proteases), rapid clearance, and immunogenicity. For some proteins, one approach to these problems has been conventional chemical pegylation the

attachment of the large, water-soluble polymer, polyethylene glycol (PEG), directly to the amino acid backbone of the protein. Pegylation increases the effective size of the drug and in some cases improves its solubility, stability, half-life and immunogenicity profile.

For some protein drugs, it has been difficult to achieve the benefits of pegylation by the conventional approach of attaching PEG directly to the protein backbone. A possible explanation is that the sites for the attachment of PEG occur at positions where the bulky PEG molecules block access to the active site on the protein or alter the conformation of the protein. This may diminish or eliminate drug activity.

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Our GlycoPEGylation technology enables us to attach a sugar molecule linked to PEG to the ends of carbohydrate structures, rather than attaching PEG directly on the protein backbone. Using enzymes, we are able to do this efficiently and selectively. By specifically linking PEG to carbohydrate structures that are remote from the protein s active site, GlycoPEGylation may preserve the bioactivity of the drug and extend its half-life. During the research stage, we attach PEGs of various molecular weights to create a family of different molecular sizes of the GlycoPEGylated protein, which we screen for optimal receptor binding and pharmacokinetic properties. We believe that significant clinical benefits may be achieved through the application of our GlycoPEGylation technology to proteins.

**Business Strategy**

Our primary business strategy is to develop next-generation protein drugs through three focused programs: our own proprietary drug program, our partnering and licensing program, and our exploratory research program.

**Neose Proprietary Drug Program**. During 2003, we focused our own proprietary drug program on the identification and development of two next-generation proprietary protein therapeutics: an improved EPO and an improved G-CSF. During 2004 and 2005, we intend to limit the number of proteins in our own proprietary drug program to two proteins, which we are prepared to develop independently into Phase II clinical studies before we require a corporate partner for further development. We may decide to substitute a different protein for our improved EPO or improved G-CSF, or both. Substitutions could occur for several reasons, including various problems that may arise in the drug development process and the timing of desirable opportunities for partnering the continuing development of these next-generation proteins. We will continue to evaluate the progress of our own proprietary drug program and appropriate partnering opportunities.

***Improved EPO***. In January 2003, we announced the selection of an improved EPO as the first target for our proprietary drug development program. EPO is prescribed to stimulate production of red blood cells, and is approved for sale in major markets around the world for the treatment of anemia associated with oncology chemotherapy, end-stage renal disease, and chronic renal insufficiency. EPO accounts for more sales worldwide than any other glycoprotein drug. Worldwide sales of the EPO category in 2002 were over $8 billion. Of this amount, approximately $5.7 billion in sales were in the U.S., approximately $1.9 billion in sales were in Europe and other countries outside Asia, and $0.8 billion in sales were in Japan and other Asian markets.

Based on preclinical studies conducted during 2002 and 2003, we believe it is feasible to develop a long-acting EPO through GlycoPEGylation. These studies suggest that the pharmacokinetic profile of EPO can be adjusted by manipulating the number of GlycoPEGylation sites and the molecular weight of the PEG that we attach to the compound. In these early studies, the biological activity of constructs of GlycoPEGylated EPO was comparable to the activity of unmodified EPO and Aranesp®, Amgen s longer acting EPO analog. Based on our preliminary market research, we believe that clinicians, particularly oncologists, would favor a long-acting EPO. This is supported by quantitative data for Aranesp, indicating that, six quarters after launch, annualized sales were greater than $1 billion.

We believe that the expiration of key patents covering EPO will provide commercial opportunities in a time frame consistent with our development timeline. We expect that regulatory approval for our improved EPO will be sought both in and outside the U.S. In Europe and Japan, the key patents will expire in the middle of this decade. In the U.S., the patent situation surrounding EPO is more complex, making the time frame less predictable. There are existing patent claims that may cover our improved EPO, and we continue to evaluate whether these patent claims will prevent our entry into the U.S. market prior to their expiration. Some of the issues relevant to our analysis are the subject of ongoing litigation between other parties. While our objective is to pursue early entry opportunities in the U.S., we expect that the first regulatory and marketing applications will be made in Europe, where the risk of patent conflict appears to be lower. We expect to complete various preclinical activities during the first half of 2004, and, if the results are successful, our goal is to initiate clinical trials by the end of 2004. We expect that data from these trials will be submitted to the appropriate government agencies for regulatory approval.

***Improved G-CSF***. In October 2003, we selected an improved G-CSF as our second proprietary drug development target. G-CSF is prescribed to stimulate production of neutrophils (a type of white blood

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cell), and is approved for sale in major markets around the world for treatment of neutropenia associated with oncology chemotherapy. Based on proof-of-concept data, we believe it is feasible to develop a long acting G-CSF through GlycoPEGylation. We are planning to continue various preclinical development activities during 2004, with the goal of initiating clinical trials in the second half of 2005. In Europe, the key patents covering G-CSF will expire in 2005. In the U.S., key patents will expire in late 2013. Nevertheless, we are evaluating early entry strategies for the U.S. market. Although it is too early to predict the likely success of these strategies, we expect that applications for regulatory and marketing approvals will be submitted first in Europe.

**Partnering and Licensing Program**. We also work in collaboration with partners to incorporate our technology in next-generation proteins. In our partnering and licensing program, we generally seek collaborations where:

- our partner supplies protein,
- we use our technologies to modify the protein and to develop manufacturing-scale reagents and protocols for production,
- our partner licenses our technologies for the development and commercialization of the modified protein,
- our partner pays for our research and development activities, and
- our partner pays development milestones and royalties on the resulting next-generation protein sales.

***Novo Nordisk***. In November 2003, we announced two new agreements with Novo Nordisk to use our technologies to develop and commercialize three next-generation versions of currently marketed proteins, one of which is marketed by Novo Nordisk. These agreements are the result of exploratory research we previously conducted with Novo Nordisk and the successful application of our GlycoPEGylation technology to three complex proteins. Under our new agreements, we received a $4.3 million upfront fee, and Novo Nordisk is funding our research and development activities for these three proteins. We may also receive up to $51.3 million in development milestones, as well as royalties on sales of the licensed products. Under these agreements, Novo Nordisk s license with respect to each protein will continue until the expiration of the last Neose patent covering a licensed product, or until the earlier termination of the applicable agreement. Novo Nordisk has the right to terminate each of the agreements without cause, after giving us 90 days notice. We have the right to terminate the agreement with respect to two of the proteins if there are no commercial sales of licensed products within a specified period of years.

**Exploratory Research Program**. We conduct exploratory research, both independently and with collaborators, to identify proteins that are likely candidates for development using our technologies. Successful candidates may be advanced for development through our own proprietary drug program or through our partnering and licensing program. In 2003, we announced two collaborative exploratory research agreements, one with Rentschler and one with Sandoz.

- Under our collaboration agreement with Rentschler, we are working on the development of a next-generation protein, using an undisclosed protein supplied by Rentschler. If Neose decides to proceed with the commercialization of this next-generation protein, Rentschler may continue to collaborate with Neose as a co-developer or as a supplier of the protein.
- Under our collaboration with Sandoz, we are working on the development of a next-generation protein, using an undisclosed protein that is supplied by Sandoz. If Neose and Sandoz decide to proceed with the commercialization of this next-generation protein, we would have co-exclusive worldwide rights.

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**Other Programs**. Since we are now focused on developing next-generation proprietary protein therapeutics through our own drug development program, our partnering and licensing program, and our exploratory research program, we are evaluating the most effective means of continuing some of the other projects we have pursued in the past. We are considering whether to continue allocating some of our resources to two of these projects during 2004:

- the development of glycolipids for treating Parkinson s disease and other neurological diseases, on which we previously collaborated with Neuronyx, Inc., and
- the development of our GlycoConjugation technology, in which we would use an enzymatic approach, similar to GlycoPEGylation, to attach therapeutic or functional compounds (rather than PEG) to the carbohydrate structures on proteins.

We are looking for opportunities to out-license the technologies we have developed in two other projects:

- our joint venture with McNeil Nutritionals (a subsidiary of Johnson & Johnson) to explore inexpensive, enzymatic production of complex carbohydrates for use as bulking agents, and
- our work with Wyeth Nutrition to develop a manufacturing process for a bioactive carbohydrate to be used as an ingredient in infant and pediatric nutritional products.

**Intellectual Property**

Our success depends on our ability to protect and use our intellectual property rights in the continued development and application of our technologies, to operate without infringing the proprietary rights of others, and to prevent others from infringing on our proprietary rights. As we pursue our strategy of developing next-generation proteins, we have increased our focus on investigating the patent protection for currently marketed proteins. We also devote significant resources to obtaining and maintaining patents, and we expect to aggressively enforce our rights if necessary, although we recognize that the scope and validity of patents is never certain.

Our patent strategy has two main components, the pursuit of a patent portfolio protecting our technologies and their anticipated application, and the evaluation of patent protection for proteins we may target for development.

**Patents and Proprietary Rights**. We have continued to file patent applications covering new developments in our technologies, including compositions and methods for enzymatically adding and modifying sugar chains on a multitude of proteins to form stable linkages between a sugar attached to a polypeptide and a water soluble polymer, therapeutic compound, targeting agent, or other biologically active molecule.

In addition to developing our own intellectual property, we seek to obtain rights to complementary intellectual property from others. We have entered into license agreements with various institutions and individuals for certain patent rights, as well as sponsored research and option agreements for the creation and possible license to us of additional intellectual property rights. We are obligated to pay royalties at varying rates based upon, among other things, levels of revenues from the sale of licensed products under our existing license agreements, and we expect to pay royalties under new license agreements for intellectual property. Generally, these agreements continue for a specified number of years or as long as any licensed patents remain in force, unless the agreements are terminated earlier.

We own 29 issued U.S. patents, and have licensed 63 issued U.S. patents from 12 institutions. In addition, we own or have licensed over 90 patent applications pending in the U.S. There are also 418 foreign patent applications pending or granted related to our owned and licensed patents. In addition, we have assigned four issued U.S. patents and 34 granted or pending foreign counterparts to Magnolia Nutritionals, our joint venture with McNeil Nutritionals (a subsidiary of Johnson & Johnson).

**Next-Generation Proteins**. To pursue our strategy of developing next-generation proteins, we must ascertain the nature, scope and expiration of existing patent claims covering proteins we may target for development. The patent coverage on these proteins and methods of making them is complex. These patents must be analyzed on a claim-by-claim basis, and we must make decisions based on our analysis of these varied claims. The patents and their expiration dates often vary from the U.S. to Europe to Japan. It is possible that we are unaware of pending patent applications that are relevant to our product candidates, either because our search did not find them or because they are not yet publicly available.

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In order to market next-generation versions of currently marketed proteins, we will have to determine the expiration dates of existing patent claims that could cover our product candidate by analyzing numerous, complex patent claims and, in some cases, judicial opinions. The analysis of patents is subject to different interpretations. Our analysis of the patent coverage surrounding both EPO and G-CSF in the U.S. has encouraged us that there may be opportunities to enter the market sooner than our competitors whose products would have different characteristics or manufacturing processes. If we pursue a strategy of early entry, litigation could result, and would be costly regardless of whether we were successful. Litigation could also result in delays in the launch of a product, even if we ultimately prevailed in the litigation.

**Nature of Protection**. The nature of patent protection in the pharmaceutical and biotechnology industry is complex, uncertain and unpredictable. The patents we seek may not issue, or may issue with a narrower scope than originally sought, and may not be valid or effectively enforceable. Even if our patents are enforceable, enforcement of our patents could be time consuming and expensive. If the claims in our pending patent applications are narrowed prior to issuance, others will have greater opportunity to circumvent or design around our patent protection.

We also have proprietary trade secrets and know-how that are not patentable or which we have chosen to maintain as secret rather than filing for patent protection. We seek to protect our secret information by entering into confidentiality agreements with employees, consultants, licensees, and potential collaboration partners. These agreements generally provide that all confidential information developed, or made known, by Neose to the other party during the relationship shall be kept confidential and may not be disclosed to third parties, except in specific circumstances. Our agreements with employees also provide that inventions made by the employee during the period of employment will be solely owned by Neose if they are the result of tasks assigned by Neose or the use of property (including intellectual property) owned or used by Neose. Our agreements with consultants generally provide that inventions conceived by the consultant while rendering consulting services to Neose will be our exclusive property.

We are aware of numerous pending and issued U.S. and foreign patent rights and other proprietary rights owned by third parties in fields related to our technologies. We will continue to expend resources to protect our own technology and seek to avoid infringing the technology of others. Patent protection obtained by others may interfere with our ability to obtain patents, or our ability to effectively employ our technologies.

**Government Regulation**

Our research and development activities, the future manufacture of reagents and products incorporating our technologies, and the marketing of these products are subject to regulation for safety and efficacy by numerous governmental authorities in the U.S. and other countries.

**Regulation of Pharmaceutical Product Candidates**. The research and development, clinical testing, manufacture and marketing of products using our technologies are subject to regulation by the U.S. Food and Drug Administration (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 manufacturing and control, safety, effectiveness, labeling, storage, record keeping, approval, advertising and promotion of therapeutic products. Product development and approval within this regulatory framework take a number of years and involve the expenditure of substantial resources. We anticipate that the development of our next-generation proprietary proteins will involve a traditional development program, including clinical trials.

In the U.S., after laboratory analysis and preclinical testing in animals, an investigational new drug application (or IND) is required to be filed with the FDA before human testing may begin. Typically, a sequential three-phase human clinical testing program is then undertaken, but the phases may overlap or be combined. Certain phases may not be necessary for a particular product. Each clinical study is conducted according to

an approved protocol after written approval is obtained from an independent Institutional Review Board, or IRB. In Phase I, small clinical trials are conducted to determine the safety of the product. In Phase II, clinical trials are conducted to assess safety, establish an acceptable dose, and gain preliminary evidence of the efficacy of the product. In Phase III, clinical trials are conducted to obtain sufficient data to establish statistically significant proof of safety and efficacy.

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The time and expense required to perform this clinical testing vary and can be substantial. The results of the preclinical and clinical testing of a biological pharmaceutical product are then submitted to the FDA in the form of a Biologics License Applications (or BLA), or for a chemical pharmaceutical product in the form of a New Drug Application (or NDA), for approval to commence commercial sales. If the application contains all pertinent information and data, the FDA will formally accept the file for review. In responding to a BLA or NDA, the FDA may grant marketing approval, request additional information, or deny the application.

No action may be taken to market any new drug or biologic product in the U.S. until an appropriate marketing application has been approved by the FDA. Even after initial FDA approval is obtained, further clinical trials may be required to provide additional data on safety and effectiveness, and will be required to gain clearance for the use of a product as a treatment for indications other than those initially approved. Side effects or adverse events that are reported during clinical trials may delay, impede, or prevent marketing approval. Similarly, adverse events that are reported after obtaining marketing approval may result in additional limitations being placed on the use of a product and, potentially, withdrawal of the product from the market.

The regulatory requirements and approval processes of countries in the European Union (EU) are similar to those in the U.S. In the EU, depending on the type of drug for which approval is sought, there are currently two potential tracks for marketing approval in member countries: mutual recognition and the centralized procedure. Typically, recombinant products are reviewed through the centralized procedure. The EU review mechanisms may ultimately lead to approval in all EU countries, but each method grants all participating countries some decision-making authority in product approval.

Sales of pharmaceutical and biopharmaceutical products in other areas of the world vary from country to country. Whether or not FDA licensure has been obtained, licensure of a product by comparable regulatory authorities in other countries must be obtained prior to marketing the product in those countries. The time required to obtain such licensure may be longer or shorter than that required for FDA approval, and regulatory authorities in other areas of the world, like the FDA, may approve or deny applications for licensure and marketing.

In addition to regulating and auditing human clinical trials, the FDA regulates and inspects equipment, facilities, and processes used in the manufacture and control of products prior to providing approval to market a product. Among other conditions for marketing approval in the U.S., the prospective manufacturer s quality control and manufacturing procedures must conform on an ongoing basis with current Good Manufacturing Practices (cGMP). Before granting marketing approval, the FDA will perform a prelicensing inspection of the facility to determine its compliance with cGMP and other rules and regulations. In complying with cGMP, manufacturers must continue to expend time, money and effort in the area of production, training and quality control to ensure full compliance. After approval of a BLA or NDA, manufacturers are subject to periodic inspections by the FDA. If, as a result of FDA inspections relating to our products or reagents, the FDA determines that our equipment, facilities, or processes do not comply with applicable FDA regulations or conditions of product approval, the FDA may seek civil, criminal, or administrative sanctions and remedies against us, including the suspension of our manufacturing operations.

Products manufactured in the U.S. for distribution abroad are subject to FDA regulations regarding export, as well as to the requirements of the country to which they are shipped. Products distributed to countries within the EU are also subject to EU regulations. The requirements of the EU and foreign countries generally cover the conduct of clinical trials, the submission, review and approval of marketing applications, and all aspects of product manufacture and marketing. These requirements may vary significantly from country to country.

We expect to manufacture enzymes, sugar nucleotides and other reagents for use by our collaborators, as well as for our own manufacturing use in the development of next-generation proprietary protein therapeutics. Our partners may be responsible for clinical and regulatory approval procedures, but we would expect to participate in this process by submitting to the FDA a drug master file developed and maintained by us that contains data concerning the manufacturing and control processes for our reagents.

**Other Regulations Affecting our Business**. We are subject to various other laws and regulations, such as those relating to safe working conditions, employee relations, employee benefits, the environment (including the use and disposal of hazardous or potentially hazardous substances), antitrust and international trade, public securities and taxation. We endeavor to comply with applicable laws and regulations. However, we recognize that this is a complex and expensive process, and that we cannot predict when changes will occur or whether they would have a material adverse effect on our operations.

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We contract with third parties for supplies and services that are critical to our business. These third parties are also subject to government regulation. The failure of any of these third parties to comply with applicable laws and regulations could cause substantial delays to our drug development timelines and have a material adverse effect on our operations.

**Third-Party Reimbursement**. Our ability and each of our collaborator s ability to successfully commercialize drug products may depend in part on the extent to which coverage and reimbursement for the cost of such products will be available from government health administration authorities, private health insurers, and other organizations. Uncertainty continues within the pharmaceutical and biotechnology industries as to the reimbursement status of new therapeutic products, and we cannot be sure that third-party reimbursement would be available for any therapeutic products that we or our collaborators might develop. Healthcare reform, especially as it relates to prescription drugs, is an area of increasing attention and a priority of many governmental officials.

**Competition**

The biotechnology and pharmaceutical industries are characterized by rapidly evolving technology and significant competition. Our competitors include pharmaceutical and biotechnology companies. In addition, many specialized biotechnology companies have formed collaborations with large, established companies to support research, development and commercialization of products that may be competitive with our current and future product candidates and technologies. Academic institutions, governmental agencies and other public and private research organizations are also conducting research activities and seeking patent protection and may commercialize competitive products or technologies on their own or through collaborations with pharmaceutical and biotechnology companies.

**Next-Generation Protein Development**. We are aware that other companies are working on the development of next-generation protein therapeutics in anticipation of the expiration of certain patent claims covering marketed proteins. Companies such as Maxygen and Applied Molecular Evolution are designing and manipulating protein structures to improve the properties of therapeutic proteins, including safety, efficacy and patient convenience. Nektar, Enzon and other companies utilize chemical pegylation technologies to increase the circulating half-life of certain proteins. Some of these companies are combining protein structure manipulation and pegylation. In addition, established large pharmaceutical and biotechnology companies are utilizing chemical pegylation technologies on their own proteins. Human Genome Sciences and BioRexis are applying in-vivo fusion technologies using albumin and other carrier proteins to increase circulating half-life and potentially improve other therapeutic properties on specific proteins. In addition, drug delivery companies such as Alkermes continue to exploit formulation technologies to improve administration and dosing of therapeutic proteins. Some of these companies have greater financial, technical, manufacturing, marketing and other resources than ours, and may be better equipped than we are to develop, market and manufacture next-generation proteins. Our product candidates will face competition from products already established in the marketplace and new therapies that may be developed by our competitors or may result from advances in biotechnology or other fields.

**Competitive Next-Generation EPO and G-CSF Products**. Other companies have programs focused on developing next-generation or improved versions of EPO and G-CSF, and some are already marketing improved versions of these products.

Amgen currently markets Aranesp®, its improved version of EPO, which has a longer circulating half-life than EPO. Amgen launched Aranesp in the last quarter of 2001 and has reported that global sales of Aranesp were approximately $1.5 billion in 2003. Roche is developing an improved EPO known as CERA (Continuous Erythropoiesis Receptor Activator). In addition, non-originator companies are applying their technologies to develop improved EPO compounds, such as: Gryphon, with its precision length polymer and chemical ligation technology; Transkaryotic Therapeutics, utilizing its gene activation technology; Human Genome Sciences, with its albumin fusion technology; ARIAD, with its gene therapy and small molecule promoter technology; and Affymax, with its synthetic EPO-like peptides.

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Amgen currently markets Neulasta®, which is a modified version of its original G-CSF product, Neupogen®. Neulasta is a chemically pegylated compound, with a longer circulating half-life than Neupogen. Amgen launched Neulasta in the first quarter of 2002 and has reported that global sales of Neulasta were approximately $1.3 billion in 2003. Other companies, such as Human Genome Sciences and Affymax, are also applying their technologies to develop next-generation versions of G-CSF.

**Follow-on Biologics (Biogenerics)**. Although a clear development and regulatory path does not currently exist for biologic products that are, or soon will be, off-patent in the U.S., Europe and Japan, we are aware that companies are pursuing the opportunity to develop and commercialize follow-on versions of currently marketed products, including EPO, G-CSF and others. Companies that are expected to work in this area include Sandoz, BioGeneriX, STADA, SICOR (now a wholly owned subsidiary of Teva Pharmaceutical Industries Ltd.) and others.

**Research and Development Services**. Although we are focused on the development of next-generation protein therapeutics, we also use our GlycoAdvance and GlycoPEGylation technologies to provide collaborative research services and product improvement opportunities to other pharmaceutical and biotechnology companies. These services compete with efforts within these companies to improve therapeutic protein profiles and expression, and services provided by other companies to improve proteins, such as chemical pegylation technology.

There are several companies that are engaged in glycobiology research. Their work includes efforts to develop better-glycosylating cell lines, optimize cell culture conditions to improve glycosylation, and generate carbohydrate therapeutics. Companies working in this area include Crucell, GLYCART, GlycoFi and Momenta. Crucell has developed human cell lines for glycoprotein production. GLYCART is pursuing the glycosylation of antibodies, and GlycoFi is focused on expressing glycoproteins in yeast systems. Momenta is utilizing sophisticated analysis and design for carbohydrate-based therapeutics.

**Manufacturing**

We have invested in the construction and validation of a manufacturing pilot plant in Horsham, PA to support our business objectives. Our goals in manufacturing are:

- to operate facilities that provide economies of scale to produce enzymes, sugar nucleotides and other reagents to support our GlycoAdvance and GlycoPEGylation technologies,
- to enable production of EPO, and our next-generation GlycoPEGylated EPO, from insect cells for preclinical and Phase I and Phase II clinical studies,
- to produce our next-generation GlycoPEGylated G-CSF for preclinical immunotoxicology studies, and
- to permit our collaborators to bring potentially improved therapeutic protein products to market faster.

Additional work may be necessary to optimize manufacturing processes for regulatory approval, including the modification of fermentation conditions, downstream protein purification, and enhancements of operational reliability.

In 2003, we completed the qualification and validation of our pilot manufacturing facility in Horsham for the production of enzymes, sugar nucleotides and other reagents in accordance with applicable U.S. Food and Drug Administration s current Good Manufacturing Practices regulations (cGMP). The facility consists of approximately 24,000 square feet of processing area and utility space. Separate areas are dedicated to sugar nucleotide processing, enzymes expressed in bacterial organisms, and enzymes expressed in fungal organisms. A fourth area was remodeled to provide cell culture growth and protein isolation in support of our manufacture of EPO in insect cells. This space is segregated into two areas to provide separate space for growth of the insect cells and amplification of baculovirus genomic constructs. Additional work may be necessary to scale the processes to provide sufficient quantities of the EPO active pharmaceutical ingredient to meet our needs for preclinical immunotoxicology studies and other work in preparation for our IND filing. We plan to supply our improved, GlycoPEGylated EPO for Phase I and Phase II clinical studies and to transfer the manufacturing process to a third-party contract manufacturer or partner for Phase III and commercial supplies.

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We continue to discover and develop improved reagents and technologies, and we plan to use our pilot plant to manufacture these reagents. In addition, our facility is expected to support the manufacture of reagents to glycosylate proteins produced from bacterial origin to potentially improve their therapeutic profile. We also plan to develop processes to GlycoPEGylate G-CSF for research and development. We will be working to secure supplies of protein on acceptable terms and to develop fermentation and purification processes for the reagents necessary to produce GlycoPEGylated G-CSF.

**Marketing, Distribution, and Sales of Proprietary Protein Products**

We intend to capitalize on the significant experience and resources of our collaborative partners to commercialize proprietary products made using our technologies. These partners generally would be responsible for much of the development, regulatory approval, sales, marketing, and distribution activities for products incorporating our technologies. However, we intend to retain some commercial rights to some proteins in select territories. If we commercialize any products on our own, we will have to establish or contract for regulatory, sales, marketing, and distribution capabilities, and we may have to supplement our development capabilities. The marketing, advertising, and promotion of any product manufactured using our technology would be subject to regulation by the FDA or other governmental agencies.

**Employees**

As of December 31, 2003, we employed 142 individuals, consisting of 104 employees engaged in research, development and manufacturing activities, 7 employees devoted to business development and licensing activities, and 31 employees devoted to corporate and administrative activities. Our scientific staff includes carbohydrate biochemists as well as scientists with expertise in organic chemistry, analytic chemistry, molecular biology, microbiology, cell biology, scale-up manufacture, and regulatory affairs. During the last year, our most substantial investments in human resources have been made in the protein development and manufacturing groups, and we expect this to continue. A significant number of our employees have prior experience with pharmaceutical or biotechnology companies, and many have specialized training in carbohydrate technology. None of our employees is covered by collective bargaining agreements. We believe we have good relations with our employees.

**Internet Address and Securities Exchange Act Filings**

Our internet address is www.neose.com. We make available through our website our annual report on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended. We make these reports and amendments available on our website as soon as practicable after filing them electronically with, or furnishing them to, the Securities and Exchange Commission.

**ITEM 2. PROPERTIES.**

We own, subject to our mortgages, approximately 50,000 square feet of cGMP manufacturing, laboratory, and corporate office space in Horsham, Pennsylvania, and we lease approximately 5,000 square feet of additional office and warehouse space in a building nearby. We lease approximately 10,000 square feet of laboratory and office space in San Diego, California. The initial term of the San Diego lease ends in March 2006, at which time we have an option to extend the lease for an additional five years.

In 2001 and 2002, we made capital expenditures of $17.4 million to provide additional cGMP manufacturing capacity in our Horsham, Pennsylvania facility. We entered into a lease agreement in 2002 for a 40,000 square foot building, which we intended to convert into laboratory and office space. Later in 2002, we suspended plans to complete these renovations. In November 2003, we resumed renovation activities on approximately 25,000 square feet of the facility, leaving approximately 15,000 square feet available for future expansion. We estimate these activities will cost approximately $6.3 million, of which approximately $1.0 million had been expended as of December 31, 2003.

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**ITEM 3. LEGAL PROCEEDINGS.**

We are not a party to any material legal proceedings.

**ITEM 4. SUBMISSION OF MATTERS TO A VOTE OF SECURITY HOLDERS.**

We did not submit any matters to a vote of security holders during the fourth quarter of 2003.

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## PART II

### ITEM 5. MARKET FOR REGISTRANT S COMMON EQUITY AND RELATED STOCKHOLDER MATTERS

Our common stock is listed on The NASDAQ Stock Market under the symbol NTEC. We commenced trading on The Nasdaq Stock Market on February 15, 1996. The following table sets forth the high and low sale prices of our common stock for the periods indicated.

| | Common Stock Price | |
|---|---|---|
| | **High** | **Low** |
| **Year Ended December 31, 2002** | | |
| First Quarter | $ 37.30 | $ 29.80 |
| Second Quarter | 32.58 | 9.07 |
| Third Quarter | 11.06 | 6.41 |
| Fourth Quarter | 14.00 | 5.90 |
| **Year Ended December 31, 2003** | | |
| First Quarter | 9.31 | 6.03 |
| Second Quarter | 12.64 | 6.88 |
| Third Quarter | 11.06 | 8.50 |
| Fourth Quarter | 9.83 | 7.20 |
| **Year Ended December 31, 2004** | | |
| First Quarter (through February 15, 2004) | 13.80 | 9.14 |

As of February 15, 2004, there were approximately 200 record holders and 3,700 beneficial holders of our common stock. We have not paid any cash dividends on our common stock and we do not anticipate paying any in the foreseeable future.

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**ITEM 6. SELECTED FINANCIAL DATA.**

The following Statements of Operations and Balance Sheet Data for the years ended December 31, 1999, 2000, 2001, 2002, and 2003, and for the period from inception (January 17, 1989) through December 31, 2003, are derived from our audited financial statements. The financial data set forth below should be read in conjunction with the sections of this Annual Report on Form 10-K entitled Management s Discussion and Analysis of Financial Condition and Results of Operations, and the financial statements and notes included elsewhere in this Form 10-K.

| | Year ended December 31, | | | | | Period from inception (January 17, 1989) to December 31, |
|---|---|---|---|---|---|---|
| | 1999 | 2000 | 2001 | 2002 | 2003 | 2003 |
| | (in thousands, except per share data) | | | | | |
| **Statements of Operations Data:** | | | | | | |
| Revenue from collaborative agreements | $ 422 | $ 4,600 | $ 1,266 | $ 4,813 | $ 1,435 | $ 18,881 |
| Operating expenses: | | | | | | |
| Research and development | 10,649 | 12,094 | 14,857 | 21,481 | 26,821 | 126,499 |
| Marketing, general and administrative | 4,520 | 5,648 | 9,374 | 12,510 | 11,148 | 60,220 |
| Total operating expenses | 15,169 | 17,742 | 24,231 | 33,991 | 37,969 | 186,719 |
| Other income | | | 6,120 | 1,653 | | 7,773 |
| Impairment of equity securities | | | | | (1,250) | (1,250) |
| Interest income, net | 1,429 | 4,642 | 3,516 | 1,108 | 103 | 15,576 |
| Net loss | $ (13,318) | $ (8,500) | $ (13,329) | $ (26,417) | $ (37,681) | $ (145,739) |
| Basic and diluted net loss per share | $ (1.25) | $ (0.63) | $ (0.95) | $ (1.85) | $ (2.14) | |
| Weighted-average shares outstanding used in computing basic and diluted loss per share | 10,678 | 13,428 | 14,032 | 14,259 | 17,611 | |

| | As of December 31, | | | | |
|---|---|---|---|---|---|
| | 1999 | 2000 | 2001 | 2002 | 2003 |
| | (in thousands) | | | | |
| **Balance Sheet Data:** | | | | | |
| Cash, cash equivalents and marketable securities | $ 33,235 | $ 94,762 | $ 76,245 | $ 41,040 | $ 53,060 |
| Total assets | 52,239 | 114,768 | 105,786 | 83,092 | 94,845 |
| Total debt and capital lease obligations | 8,300 | 7,300 | 6,200 | 7,411 | 10,601 |
| Deficit accumulated during the development stage | (59,812) | (68,312) | (81,641) | (108,058) | (145,739) |

| | | | | | |
|---|---|---|---|---|---|
| Total stockholders equity | 40,785 | 104,868 | 93,946 | 70,685 | 72,213 |

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**ITEM 7. MANAGEMENT S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS.**

The following discussion should be read in conjunction with our financial statements and related notes included in this Form 10-K.

**Overview**

We are a biopharmaceutical company focused on improving protein therapeutics using our proprietary technologies. Our core technologies, GlycoAdvance and GlycoPEGylation, enable us to manipulate, enzymatically, the carbohydrate structures of glycoproteins, and thereby pursue the objective of improving the therapeutic profiles of proteins that have already been marketed or substantially developed. Our business strategy is to use our technologies to improve proteins for which there exists a substantial body of data demonstrating safety and efficacy. We intend to apply this strategy to next-generation products that we are developing on our own or in collaboration with others. We also expect to use our technologies, through strategic partners, to improve products of other parties.

We have incurred operating losses each year since our inception. As of December 31, 2003, we had an accumulated deficit of approximately $145.7 million. We expect additional losses in 2004 and over the next several years as we expand product research and development efforts, increase manufacturing scale-up activities and, potentially, begin sales and marketing activities. We have financed our operations through private and public offerings of equity securities, proceeds from debt financings, and revenues from our collaborative agreements.

We believe that our existing cash, cash equivalents, and marketable securities, expected revenue from collaborations and license arrangements, expected proceeds under the credit agreement we entered into in January 2004, and interest income should be sufficient to meet our operating and capital requirements into 2005, although changes in our collaborative relationships or our business, whether or not initiated by us, may cause us to deplete our cash and marketable securities sooner than the above estimate. Under the terms of a credit agreement we entered into in January 2004 to borrow up to $9.0 million, all of which we expect to borrow during the first quarter of 2004, we have agreed to limit our total outstanding debt to $22.0 million. After using a portion of the proceeds to repay existing debt, our total debt outstanding will be approximately $15.7 million. At any time after the fourth year of the ten-year loan period, or if we fail to maintain a minimum required cash and short-term investments balance of at least $22.0 million, the bank has the option to require additional collateral from us in the form of a letter of credit, which may have the effect of requiring us to repay the outstanding loan balance to the bank, or a security interest in certain cash and short-term investments. See Long-term Debt Other Arrangements Credit Agreement in the Liquidity and Capital Resources section of this Form 10-K for a description of the material features of this borrowing.

**Liquidity and Capital Resources**

*Overview*

We had $53,060,000 in cash, cash equivalents and marketable securities as of December 31, 2003, compared to approximately $41,040,000 in cash and cash equivalents as of December 31, 2002. The increase for 2003 was primarily attributable to the proceeds of equity and debt financings, which were offset by the use of cash to fund our operating activities, capital expenditures, and debt repayments.

The development of next-generation proprietary protein therapeutics, which we are pursuing both independently and in collaboration with selected partners, will require substantial expenditures by us and our collaborators. To finance those expenditures, we plan to continue financing our operations through private and public offerings of equity securities, proceeds from debt financings, and revenues from existing and future collaborative agreements. Our 2004 revenues are difficult to project and will be largely dependent on entering into new collaborations and on the financial terms of any new collaborations. Other than revenues from our collaboration with Novo Nordisk, and any future collaborations with others, we expect to generate no significant revenues until such time as products incorporating our technologies are commercialized, which is not expected during the next

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several years. We expect an additional several years to elapse before we can expect to generate sufficient cash flow from operations to fund our operating and investing requirements. Accordingly, we will need to raise substantial additional funds to continue our business activities and fund our operations beyond 2004.

*Significant 2003 Cash Flows and Proceeds from Sales of Equity*

During 2003, our operating activities consumed $27,476,000, which included the receipt of a nonrefundable, upfront fee of $4,300,000 upon entering into our collaboration with Novo Nordisk. In addition, we invested $3,455,000 in capital expenditures, and made debt principal repayments of $2,584,000. To finance these and future expenditures, we received $38,893,000 from public and private offerings of our common stock and $4,987,000 in proceeds from debt financings. We also entered into capital lease obligations during 2003 for assets with aggregate book values of $787,000.

In September 2003, we sold 2,655,557 shares of common stock in a registered offering to a group of institutional and individual investors, generating net proceeds of $22,377,000. In February 2003, we sold 2,866,763 shares of common stock in a private placement to a group of institutional and individual investors, generating net proceeds of $16,320,000. In addition, employees purchased 25,836 shares of common stock during 2003 pursuant to our employee stock purchase plan, resulting in net proceeds of $196,000. During 2003, we received proceeds of $172,000 upon the exercise of options to purchase 62,780 shares of common stock.

*Long-term Debt Proceeds from 2003 Arrangements*

In this section, we describe the material features of our new issuances of debt, and capital lease obligations entered into, during 2003. In the following section, Long-term Debt Other Arrangements , we describe the material features of long-term debt arrangements that did not involve new borrowings during 2003, including a significant new agreement that we entered into in January 2004 to borrow up to $9,000,000, all of which we expect to borrow during the first quarter of 2004.

*2003 Equipment Loans*

In December 2003, we borrowed $1,201,000 to finance the purchase of equipment and facility improvements, which collateralize the amount borrowed. The terms of the financing require us to pay monthly principal and interest payments over 48 months at an interest rate of 8.66%. During 2004, we will be required to make principal and interest payments totaling $335,000 under this agreement.

In September 2003, we borrowed $831,000 to finance the purchase of equipment and facility improvements, which collateralize the amount borrowed. The terms of the financing require us to pay monthly principal and interest payments over 48 months at an interest rate of 8.35%. During 2004, we will be required to make principal and interest payments totaling $269,000 under this agreement.

In March 2003, we borrowed $2,954,000 to finance the purchase of equipment, which collateralize the amount borrowed. The terms of the financing require us to pay monthly principal and interest payments over 42 months at an interest rate of 8.35%. During 2004, we will be

required to make principal and interest payments totaling $976,000 under this agreement.

*2003 Capital Lease Obligations*

In September 2003, we entered into a capital lease for $354,000 of equipment. The terms of the lease required us to make an initial payment of $90,000 followed by monthly payments through September 2006. During 2004, we will be required to make lease payments totaling $99,000 under this agreement. We also entered into a capital lease obligation during September 2003 for $60,000 of software. The terms of the lease require us to make monthly payments through September 2008. During 2004, we will be required to make lease payments totaling $16,000 under this agreement.

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In June 2003, we entered into a capital lease for $119,000 of equipment. The terms of the lease required us to make an initial payment of $31,000 followed by monthly payments through June 2006. During 2004, we will be required to make lease payments totaling $37,000 under this agreement.

In April and May 2003, we entered into capital leases for $254,000 of equipment. The terms of the leases require us to make monthly payments through April 2006. During 2004, we will be required to make lease payments totaling $96,000 under these agreements.

*Long-term Debt Other Arrangements*

In this section, we describe the material features of our debt arrangements that did not involve new borrowings during 2003, including a significant new agreement that we entered into in January 2004 to borrow up to $9,000,000, all of which we expect to borrow during the first quarter of 2004. In the previous section, Long-term Debt Proceeds from 2003 Arrangements, we describe the material features of long-term debt arrangements entered into during 2003.

*Credit Agreement*

In January 2004, we borrowed $6,200,000 from a bank for the purpose of funding improvements to our leased facility in Horsham, PA. The credit agreement with our bank provides for us to borrow from the bank an additional $1,800,000 and to utilize $1,100,000 of our restricted cash for the purpose of paying in full the $2,900,000 outstanding of our taxable Industrial Development Authority bonds, which payment we expect to occur during the first quarter of 2004. During the first quarter of 2004, we expect to enter into another agreement with the bank for it to acquire and reissue the $1,000,000 outstanding of our tax-exempt Industrial Development Authority bonds. If the tax-exempt bond acquisition described above does not occur, the existing credit agreement provides for us to borrow an additional $1,000,000 for the purpose of paying in full the outstanding amount of the tax-exempt Industrial Development Authority bonds.

Initially, the interest rate on the bonds will vary quarterly, depending on LIBOR rates. We will have the option each quarter to bear interest on the outstanding principal at a LIBOR-based variable interest rate or a fixed rate offered by our bank.

If the tax-exempt bond acquisition described above occurs, we will make quarterly, interest-only payments on the related $1,000,000 debt for ten years followed by a single repayment of principal at the end of the ten-year loan period. For the debt outstanding under the existing credit agreement, we will make quarterly, interest-only payments through March 31, 2005. Commencing on March 31, 2005, we will make quarterly principal and interest payments over the remaining nine years of the ten-year loan period. The outstanding debt will be $8,000,000 if the tax-exempt bond acquisition described above occurs and $9,000,000 if the tax-exempt bond acquisition described above does not occur.

To provide credit support for the agreement, we granted a second mortgage to our bank on the land and building where our present headquarters are located, as well as on improvements, certain equipment, and other tangible personal property. The second mortgage will automatically convert to a first mortgage upon payment in full of our Industrial Development Authority Bonds, which payment we expect to occur during the first quarter of 2004. In the credit agreement, we agreed to limit our total outstanding debt to $22,000,000. After using a portion of the proceeds to repay existing debt, our total debt outstanding will be approximately $15,700,000. At any time after the fourth year of the loan period, or if we fail to maintain a minimum required cash and short-term investments balance of at least $22,000,000, the bank has the option to require additional collateral from us in the form of a letter of credit or a security interest in certain cash and short-term investments.

*Montgomery County (Pennsylvania) IDA Bonds*

In 1997, we issued, through the Montgomery County (Pennsylvania) Industrial Development Authority, $9,400,000 of taxable and tax-exempt bonds, of which $3,900,000 remains outstanding as of December 31, 2003. As mentioned above, we expect during the first quarter of 2004 to pay in full the outstanding loan balance of the taxable bonds and to have our bank acquire and reissue the tax-exempt bonds. The bonds were

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issued to finance the purchase of our headquarters building and the construction of a pilot-scale manufacturing facility within our building. The bonds are supported by an AA-rated letter of credit, and a reimbursement agreement between our bank and the letter of credit issuer. The interest rate on the bonds varies weekly, depending on market rates for AA-rated taxable and tax-exempt obligations, respectively. During 2003, the weighted-average, effective interest rate was 2.7% per year, including letter-of-credit and other fees. The terms of the bond issuance provide for monthly, interest-only payments and a single repayment of principal at the end of the twenty-year life of the bonds. However, under our agreement with our bank, we make monthly payments to an escrow account to provide for an annual prepayment of principal. As of December 31, 2003, we had restricted funds relating to the taxable bonds of $901,000, which consisted of our monthly payments to an escrow account plus interest revenue on the balance of the escrow account. During the first quarter of 2004, we expect to use the restricted funds and a portion of the proceeds under the credit agreement we entered into in January 2004 to pay in full the outstanding balance of the taxable bonds.

To provide credit support for this arrangement, we granted a first mortgage on the land, building, improvements, and certain machinery and equipment to our bank. We also agreed to maintain a minimum required cash and short-term investments balance of at least two times the outstanding loan balance. If we fail to comply with this requirement, we are required to deposit with the lender cash collateral up to, but not more than, the unpaid balance of the loan. At December 31, 2003, we were required to maintain $7,800,000 of cash and short-term investments.

*2002 Arrangements*

In December 2002, we borrowed approximately $2,261,000 to finance the purchase of equipment, which collateralize the amount borrowed. The terms of the financing require us to pay monthly principal and interest payments over 36 months at an interest rate of 8.0%. During 2004, we will be required to make principal and interest payments totaling $850,000 under this agreement.

In November 2002, we entered into a capital lease for $50,000 of equipment. The terms of the lease require us to make monthly payments over 36 months. During 2004, we will be required to make payments totaling $19,000 under this agreement.

*Capital Expenditures*

During 2001, 2002, and 2003, we purchased $9,371,000, $17,826,000, and $3,455,000, respectively, of property, equipment, and building improvements. In addition, during 2002 and 2003 we entered into capital lease obligations for assets with aggregate book values of $50,000 and $787,000, respectively. Our capital expenditures during 2001 and 2002 consisted largely of the two following facility improvement projects:

We completed construction in 2002 of a pilot manufacturing facility at our headquarters location for the production of enzymes and sugar nucleotides at commercial-scale in accordance with applicable U.S. Food and Drug Administration s current Good Manufacturing Practices regulations. The facility comprises approximately 20,000 square feet of processing areas and 3,500 square feet of utility space. It has bacterial and fungal fermentation capabilities and houses two 1,500 liter fermenters. We expended approximately $17,448,000 for this project, of which $8,197,000 and $9,251,000 were expended in 2001 and 2002, respectively.

We entered into a lease agreement in 2002 for a 40,000 square foot building, which we intended to convert into laboratory and office space. Later in 2002, we suspended plans to complete these renovations. In November 2003, we reinitiated renovation activities at an expected additional cost of $6,300,000, which is incremental to $4,081,000 previously invested in these renovations, on approximately 25,000 square feet of the facility, leaving approximately 15,000 square feet available for future expansion. Our construction-in-progress at December 31, 2002 and 2003 includes $3,992,000 and $5,091,000, respectively, in renovations to this

facility. In January 2004, we borrowed $6,200,000 from a bank for the purpose of funding these improvements. See Long-term Debt Other Arrangements Credit Agreement in the Liquidity and Capital Resources section of this Form 10-K for a description of the material features of this borrowing.

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In 2004, we expect our investment in capital expenditures to be approximately $10.0 million, which includes the impact of resuming the facility renovations described above. In addition to the credit agreement described above, we may finance some or all of these capital expenditures through capital leases or the issuance of new debt or equity. If we issue new debt, we may be required to maintain a minimum cash and investments balance, or to transfer cash into an escrow account to collateralize some portion of the debt, or both.

*Summary of Contractual Obligations*

See Long-term Debt Other Arrangements Credit Agreement in the Liquidity and Capital Resources section of this Form 10-K for a description of the material features, including our repayment obligations, of the credit agreement we entered into in January 2004. The following table summarizes our obligations to make future payments under current contracts as of December 31, 2003:

| | Payments due by period | | | | |
|---|---|---|---|---|---|
| | Total | Less than 1 Year | 1 - 3 Years | 4 - 5 Years | After 5 Years |
| Long-term debt[1] | $ 9,982,000 | $ 2,008,000 | $ 5,400,000 | $ 2,230,000 | $ 344,000 |
| Capital lease obligations[2] | 619,000 | 223,000 | 371,000 | 25,000 | |
| Operating leases[3] | 10,125,000 | 792,000 | 1,287,000 | 899,000 | 7,147,000 |
| Purchase obligations[4] | 1,999,000 | 1,660,000 | 299,000 | 40,000 | |
| Other long-term liabilities reflected on our balance sheet under GAAP[5] | 794,000 | 531,000 | 263,000 | | |
| Total contractual obligations | $ 23,519,000 | $ 5,214,000 | $ 7,620,000 | $ 3,194,000 | $ 7,491,000 |

1. See Long-term debt in this Liquidity and Capital Resources section for a description of the material features of our long-term debt. Because we expect to refinance our Industrial Development Authority bonds during the first quarter of 2004 under a credit agreement entered into in January 2004, we have adjusted the minimum principal repayments relating to the bonds to reflect the principal repayment schedule of the new debt. See Note 7 of the Notes to Financial Statements included in this Form 10-K.
2. See Capital Lease Obligations and Note 7 of the Notes to Financial Statements included in this Form 10-K in this Liquidity and Capital Resources section for a description of the material features of our capital lease obligations.
3. See Note 14 of the Notes to Financial Statements included in this Form 10-K for a description of our significant operating leases. The obligations presented in this table include $151,000 of deferred rent, which is included in the Other Liabilities section of our Balance Sheet.
4. Includes our commitments as of December 31, 2003 to purchase goods and services.
5. Represents the present value as of December 31, 2003 of the remaining payments under agreements with two former employees. These agreements are described in Note 12 of the Notes to Financial Statements included in this Form 10-K.

**Off-Balance Sheet Arrangements**

We are not involved in any off-balance sheet arrangements that have or are reasonably likely to have a material future effect on our financial condition, changes in financial condition, revenues or expenses, results of operations, liquidity, capital expenditures, or capital resources.

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**Critical Accounting Policies and Estimates**

Our Management s Discussion and Analysis of Financial Condition and Results of Operations ( MD&A ) focuses on our liquidity, capital resources, and financial statements. The financial statements have been prepared in accordance with accounting principles generally accepted in the U.S. The preparation of financial statements requires management to make estimates and assumptions that affect the carrying amounts of assets and liabilities, and the reported amounts of revenues and expenses during the reporting period. These estimates and assumptions are developed and adjusted periodically by management based on historical experience and on various other factors that are believed to be reasonable under the circumstances. Actual results may differ from these estimates.

Our summary of significant accounting policies is described in Note 2 to our financial statements included in Item 8 of this Form 10-K. Management considers the following policies and estimates to be the most critical in understanding the more complex judgments that are involved in preparing our financial statements and the uncertainties that could impact our results of operations, financial position, and cash flows. Management has discussed the development and selection of these critical accounting policies and estimates with the audit committee of our board of directors, and the audit committee has reviewed the company s disclosure relating to it in this MD&A.

*Valuation of Long-Lived Assets*

We evaluate our long-lived assets for impairment whenever indicators of impairment exist. Our history of negative operating cash flows is an indicator of impairment. Accounting standards require that if the sum of the future cash flows expected to result from a company s long-lived asset, undiscounted and without interest charges, is less than the reported value of the asset, an asset impairment must be recognized in the financial statements. The amount of the recognized impairment would be calculated by subtracting the fair value of the asset from the reported value of the asset.

*Valuation of Acquired Intellectual Property*

The carrying value of acquired intellectual property ( Acquired IP ) on our balance sheet as of December 31, 2003 was $1.9 million. We reviewed our acquired intellectual property ( Acquired IP ) for impairment as of December 31, 2003. Because the undiscounted sum of the estimated future cash flows from the Acquired IP exceeded the carrying value, we have not recognized an impairment.

We believe that the accounting estimate related to asset impairment of our Acquired IP is a critical accounting estimate because:

- the accounting estimate is highly susceptible to change from period to period because it requires company management to estimate future cash flows over the life of our Acquired IP by making assumptions about the timing and probability of our success in:
  - entering into new collaborations; and
  - developing and commercializing products that incorporate our technologies, either directly or with collaborators; and

the recognition of an impairment would have a material impact on the assets reported on our balance sheet as well as our net loss.

Management s assumptions underlying the estimate of cash flows require significant judgment because we have limited experience in entering into collaborations with others to develop products incorporating our technologies. In addition, we have limited experience in developing products incorporating our technologies and we have no experience in commercializing any products.

In estimating the impact of future collaborations, we have made assumptions about the timing of entering into collaborations for potential products, most of which we are not yet developing. We have used data from public and private sources to estimate the types of cash flows that would occur at various stages of development for each product.

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As of December 31, 2003, we estimate that our future cash flows, on an undiscounted basis, related to Acquired IP are greater than the current carrying value of the asset. Any decreases in estimated future cash flows could have an impact on the carrying value of the Acquired IP. If we had determined the Acquired IP to be fully impaired as of December 31, 2003, total assets would have been reduced by 2% and net loss would have been increased by 5%.

*Valuation of Property and Equipment*

Our property and equipment, which have a carrying value of $37.2 million as of December 31, 2003, have been recorded at cost and are being amortized on a straight-line basis over the estimated useful lives of those assets. Approximately $5.2 million of the carrying value represents the cost and, we believe, the fair value of construction-in-progress. We believe the remaining property and equipment carrying value of $32.0 million does not exceed its fair value.

*Valuation of Investment in Convertible Preferred Stock*

In 2000, we made an investment of $1,250,000 in convertible preferred stock of Neuronyx, Inc., and entered into a research and development collaboration with Neuronyx for the discovery and development of drugs for treating Parkinson s disease and other neurological diseases. We recorded the equity investment at cost. In October 2003, Neuronyx informed us that they had completed an equity financing, under which other Neuronyx investors have an aggregate liquidation preference that is senior to our liquidation preference and exceeds the post-money valuation of Neuronyx. As a result, we reduced the carrying value of our equity investment to zero as of September 30, 2003 by recording a non-cash charge, which is reflected as an impairment of equity securities in our statements of operations.

*Revenue Recognition*

Our revenue from collaborative agreements consists of upfront fees, research and development funding, and milestone payments. We recognize revenues consistent with Staff Accounting Bulletin No. 104, Revenue Recognition (SAB 104). SAB 104 was issued by the Securities and Exchange Commission in December 2004, and updates the guidance from Staff Accounting Bulletin No. 101, Revenue Recognition in Financial Statements. Non-refundable upfront fees are deferred and amortized to revenue over the related performance period. We estimate our performance period based on the specific terms of each collaborative agreement, but the actual performance period may vary. We adjust the performance periods based on available facts and circumstances. Periodic payments for research and development activities are recognized over the period that we perform those activities under the terms of each agreement. Revenue resulting from the achievement of milestone events stipulated in the agreements is recognized when the milestone is achieved. Milestones are based on the occurrence of a substantive element specified in the contract or as a measure of substantive progress towards completion under the contract.

In November 2003, we entered into two research, development and license agreements with Novo Nordisk A/S to use our GlycoPEGylation technology to develop three next-generation proteins within Novo Nordisk s therapeutic areas, one of which is currently marketed by them. Under the terms of the new agreements, we received a non-refundable, upfront fee of $4,300,000. As required under SAB 104, we deferred the upfront fee and will amortize this amount over an expected performance period of five years. Our estimate of the performance period is a critical accounting estimate because:

the accounting estimate is highly susceptible to change from period to period (because the estimate depends on the preclinical and clinical progress of the three next-generation proteins); and

a change in the expected performance period could have a material impact on the deferred revenue reported on our balance sheet as well as our net loss.

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*Stock-based Employee Compensation*

We apply APB Opinion No. 25, Accounting for Stock Issued to Employees (APB 25), and related interpretations in accounting for all stock-based employee compensation. We record deferred compensation for option grants to employees for the amount, if any, by which the market price per share exceeds the exercise price per share. We amortize deferred compensation over the vesting periods of each option.

We have elected to adopt only the disclosure provisions of Statement of Financial Accounting Standards No. 123, Accounting for Stock-Based Compensation (SFAS 123), as amended by Statement of Financial Accounting Standards No. 148, Accounting for Stock-Based Compensation Transition and Disclosure. The following table illustrates the effect on our net loss and basic and diluted net loss per share if we had recorded compensation expense for the estimated fair value of our stock-based employee compensation, consistent with SFAS 123 (in thousands, except per share data):

| Year Ended December 31, | 2001 | 2002 | 2003 |
|---|---|---|---|
| Net loss as reported | $ (13,329) | $ (26,417) | $ (37,681) |
| Add: Stock-based employee compensation expense included in reported net loss | 125 | 171 | 100 |
| Deduct: Total stock-based employee compensation expense determined under fair value-based method for all awards | (8,179) | (15,588) | (11,893) |
| Net loss pro forma | $ (21,383) | $ (41,834) | $ (49,474) |
| Basic and diluted net loss per share as reported | $ (0.95) | $ (1.85) | $ (2.14) |
| Basic and diluted net loss per share pro forma | $ (1.52) | $ (2.94) | $ (2.81) |

**Results of Operations**

*Years Ended December 31, 2003 and 2002 and Outlook for 2004*

Our net loss for the year ended December 31, 2003 was $37,681,000 compared to $26,417,000 for the corresponding period in 2002. The following section explains the trends within each component of net loss for 2003 compared to 2002 and provides our estimate of trends for 2004 for each component.

Revenue from Collaborative Agreements. Revenues from collaborative agreements decreased to $1,435,000 in 2003 from $4,813,000 in 2002. Our revenues from collaborative agreements have historically been derived from a few major collaborators. Our collaborative agreements provide for some or all of the following elements: upfront fees, research and development funding, milestone revenues, and royalties on product sales.

In November 2003, we entered into two research, development and license agreements with Novo Nordisk A/S. Under the terms of the new agreements, we received a non-refundable, upfront fee of $4,300,000. As required under SAB 104, we deferred the upfront fee and will amortize this amount over an average expected performance period of five years. During the year ended December 31, 2003, Novo Nordisk accounted for

$694,000 of our revenues, of which $107,000 represented amortization of the upfront fee.

During 2002 and 2003, Wyeth accounted for revenues of $4,472,000 and $250,000, respectively. Our collaboration with Wyeth Pharmaceuticals was terminated in September 2002, and we expect to receive no further revenues under this agreement. During 2003, we completed activities related to our Wyeth Nutrition collaboration and recorded as revenue the last scheduled payment for research and development funding of $250,000, which we received in October 2002. Separately, we recognized revenue during 2003 of $400,000 under a license agreement.

Because our 2004 revenues could be substantially affected by entering into new collaborations and on the financial terms of any new collaborations, we cannot estimate our 2004 revenues.

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*Research and Development Expense*. In January 2003, we announced the selection of an improved erythropoietin (EPO) as the target for our first proprietary drug development project. EPO is prescribed to stimulate production of red blood cells, and is approved for sale in major markets around the world for the treatment of anemia associated with oncology chemotherapy, end stage renal disease, and chronic renal insufficiency. Based on proof-of-concept data, we believe it is feasible to develop a long acting EPO through GlycoPEGylation. We expect to complete various preclinical activities during the first half of 2004, and our goal is to initiate clinical trials by the end of 2004.

In October 2003, we announced the selection of an improved granulocyte colony stimulating factor (G-CSF) as the target for our second proprietary drug development project. G-CSF is prescribed to stimulate production of neutrophils (a type of white blood cell), and is approved for sale in major markets around the world for treatment of neutropenia associated with oncology chemotherapy. Based on proof-of-concept data, we believe it is feasible to develop a long acting G-CSF through GlycoPEGylation. We are planning to continue various preclinical development activities during 2004, with the goal of initiating clinical trials by the end of 2005.

We are working in collaboration with Novo Nordisk to incorporate our technology in three next-generation versions of marketed proteins, one of which is currently marketed by Novo Nordisk. We are also conducting exploratory research, both independently and with collaborators, to identify proteins that are likely candidates for development using our technologies, which may be advanced for development through our own proprietary drug program or through our partnering and licensing program. We are continuing some work on the development of our other programs, including new applications of our GlycoPEGylation and GlycoConjugation technologies.

Our current research and development projects are divided between two categories: (i) GlycoAdvance and GlycoPEGylation and (ii) Other Glycotechnology Programs, which includes projects investigating other applications of our intellectual property. We are exploring the most cost-effective means of continuing some of the projects classified as Other Glycotechnology Programs. The following chart sets forth our projects in each of these categories and the stage to which each has been developed:

| | Development Stage | Status |
|---|---|---|
| **GlycoAdvance and GlycoPEGylation** | | |
| Improved erythropoietin | Preclinical | Active |
| Improved granulocyte colony stimulating factor | Preclinical | Active |
| | Research | Active |
| Other protein projects | | |
| **Other Glycotechnology Programs** | | |
| Non-protein therapeutic applications | Research | Active |
| Nutritional applications | N/A | Evaluating outlicensing opportunities |

For each of our research and development projects, we incur both direct and indirect expenses. Direct expenses include salaries and other costs of personnel, raw materials, and supplies for each project. We may also incur third-party costs related to these projects, such as contract research, consulting and preclinical development costs. Indirect expenses include depreciation expense and the costs of operating and maintaining our facilities, property, and equipment, to the extent used for our research and development projects, as well as the costs of general management of our research and development projects.

Our research and development expenses increased to $26,821,000 in 2003 from $21,481,000 in 2002. We expect our research and development expenses to be significantly greater in 2004 than they were in 2003, as a result of the development, preclinical and clinical activities we plan to conduct during the year. The following table illustrates research and development expenses incurred during 2002 and 2003 in each period for our significant groups of research and development projects (in thousands).

| **Year Ended December 31,** | **2002** | **2003** |
|---|---|---|
| GlycoAdvance and GlycoPEGylation | $ 7,082 | $ 10,012 |
| Other Glycotechnology Programs | 1,779 | 486 |
| Indirect expenses | 12,620 | 16,323 |
| | $ 21,481 | $ 26,821 |

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*GlycoAdvance and GlycoPEGylation*

Our GlycoAdvance and GlycoPEGylation research and development expenses increased during 2003, compared to 2002, primarily due to increased preclinical development costs associated with our improved EPO, purchases of laboratory services and research supplies, including proteins, and the reallocation of resources from our Other Glycotechnology Programs.

*Other Glycotechnology Programs*

Research and development expenses related to our Other Glycotechnology Programs decreased during 2003, compared to 2002, consistent with our decision during 2002 to focus our resources on our GlycoAdvance and GlycoPEGylation programs.

*Indirect expenses*

Our indirect research and development expenses increased during 2003, compared to 2002, primarily due to increases related to depreciation of pilot manufacturing facility improvements, which were placed in service in January 2003, additional personnel, and the purchase of more supplies and outside services than in 2002. Substantially offsetting these increases was a reduction in severance expense during 2003 of $2,294,000, of which $1,608,000 was a non-cash charge, related to an agreement entered into during the first quarter of 2002 with one of our former executive officers.

The process of bringing drugs from the preclinical research and development stage through Phase I, Phase II, and Phase III clinical trials and FDA approval is a time consuming and expensive process. Because our announced product candidates are currently in the preclinical stage and there are a variety of potential intermediate clinical outcomes that are inherent in drug development, we cannot reasonably estimate the timing and costs we will incur to complete these research and development projects. In addition, the timing and costs to complete our research and development projects will be affected by the timing and nature of any collaboration agreements we may enter into with a third party, neither of which we can currently estimate.

Material cash inflows from proprietary drug development projects are highly uncertain, and we cannot reasonably estimate the period in which we will begin to receive material net cash inflows from our major research and development projects. Cash inflows from development-stage products are dependent on several factors, including entering into collaborative agreements, the achievement of certain milestones, and regulatory approvals. We may not receive milestone payments from any existing or future collaborations if a development-stage product fails to meet technical or performance targets or fails to obtain the required regulatory approvals. Further, our revenues from collaborations will be affected by the level of efforts committed and made by our collaborative partners. Even if we achieve technical success in developing drug candidates, our collaborative partners may not devote the resources necessary to complete development and commence marketing of these products or they may not successfully market potential products.

*Marketing, General and Administrative Expense*. Marketing, general and administrative expenses for the year ended December 31, 2003 were $11,148,000, compared to $12,510,000 for the corresponding period in 2002. The 2002 period contained higher consulting expenses and costs associated with executive recruitment and relocation than the comparable 2003 period. The decreases in those expenses during 2003 were partly offset by increases in payroll. During 2004, we expect our marketing, general and administrative expenses to increase by less than 10% over 2003.

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*Other Income and Expense.* During the year ended December 31, 2003, we recorded a non-cash impairment charge of $1,250,000 relating to our investment in Series A convertible preferred stock of Neuronyx, Inc. We recorded the equity investment, which was made in 2000, at cost. In October 2003, Neuronyx informed us they were nearing completion of a Series C equity financing, under which Series C and Series B Neuronyx investors would have an aggregate liquidation preference that is senior to the Series A liquidation preference and exceeds the assumed post-money valuation of Neuronyx. As a result, we reduced the carrying value of our equity investment to zero as of September 30, 2003 by recording the non-cash impairment charge.

During the year ended December 31, 2002, we recognized $1,653,000 of other income upon receipt from Genzyme General of a contract payment, which was due as a result of the restructuring of our agreement with Novazyme Pharmaceuticals, Inc. in March 2001. In September 2001, Genzyme acquired Novazyme, and assumed Novazyme s contractual obligation to us. We did not recognize any other income during 2003.

Interest income for the year ended December 31, 2003 was $564,000, compared to $1,108,000 for the corresponding period in 2002. The decrease was due to lower average cash and cash equivalents and marketable securities balances, as well as lower interest rates, during 2003. Our interest income during 2004 is difficult to project, and will depend largely on prevailing interest rates and whether we complete any collaborative agreements and any additional equity or debt financings during the year.

Interest expense for the year ended December 31, 2003 was $461,000, compared to zero for the corresponding period in 2002. In 2002, we capitalized $150,000 of interest expense on our two capital construction projects, as discussed in the Liquidity and Capital Resources section of this MD&A. In accordance with GAAP, we recognized capitalized interest for these projects only to the extent of our actual interest expense, resulting in no reported interest expense for 2002. We expect our interest expense during 2004 to increase due to our entering into an agreement in January 2004 to borrow up to $9,000,000, all of which we expect to borrow during the first quarter of 2004. See Long-term Debt Other Arrangements Credit Agreement in the Liquidity and Capital Resources section of this Form 10-K for a description of the material features of this debt financing.

*Years Ended December 31, 2002 and 2001*

Our net loss for the year ended December 31, 2002 was $26,417,000 compared to $13,329,000 for the corresponding period in 2001. The following section explains the trends within each component of net loss for 2002 compared to 2001.

*Revenue from Collaborative Agreements.* Revenues from collaborative agreements increased to $4,813,000 in 2002 from $1,266,000 in 2001. The increase in revenues during 2002 was primarily a result of our Wyeth Pharmaceuticals collaboration, which was terminated in the third quarter of 2002. Of the increase, $1,000,000 was non-cash, and represented the remaining amortization of the upfront fee that Wyeth paid in December 2001. As required under SAB 101, we deferred the upfront fee and began to amortize this amount as revenue over the expected performance period of the Wyeth agreement. Upon termination of the Wyeth agreement, the unamortized portion of the upfront fee was recognized as revenue.

*Research and Development Expense.* Research and development expenses for the year ended December 31, 2002 were $21,481,000, compared to $14,857,000 for the year ended December 31, 2001. The following table illustrates research and development expenses incurred during 2001 and 2002 in each period for our significant groups of research and development projects (in thousands).

| Year Ended December 31, | 2001 | 2002 |
|---|---|---|
| GlycoAdvance and GlycoPEGylation | $ 3,066 | $ 7,082 |
| Other Glycotechnology Programs | 2,690 | 1,779 |
| Indirect expenses | 9,101 | 12,620 |
| | $ 14,857 | $ 21,481 |

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*GlycoAdvance and GlycoPEGylation*

Our GlycoAdvance and GlycoPEGylation research and development expenses increased during 2002, compared to 2001, primarily due to increased purchases of proteins, hiring of employees, and the reallocation of resources from our Other Glycotechnology Programs.

*Other Glycotechnology Programs*

Research and development expenses related to our Other Glycotechnology Programs decreased during 2002, compared to 2001, consistent with our decision during 2002 to focus our resources on our GlycoAdvance and GlycoPEGylation programs.

*Indirect expenses*

Our indirect research and development expenses increased during 2002, compared to 2001, primarily due to increases related to severance expense and costs associated with employee recruitment and relocation. During 2002, we recorded severance expense related to research and development personnel of $2,294,000, of which $1,608,000 was a non-cash charge, related to an agreement entered into during the first quarter of 2002 with one of our former executive officers.

*Marketing, General and Administrative Expense.* Marketing, general and administrative expenses for the year ended December 31, 2002 were $12,510,000, compared to $9,374,000 for the corresponding period in 2001. The 2002 period contained higher personnel costs (including payroll, recruiting, and relocation), legal, and consulting expenses than the comparable 2001 period, which increases resulted primarily from recruiting of senior executives and focusing our business on the development of next-generation proprietary protein therapeutics.

*Other Income and Expense.* During the year ended December 31, 2002, we recognized $1,653,000 of other income upon receipt from Genzyme General of a contract payment, which was due as a result of the restructuring of our agreement with Novazyme Pharmaceuticals, Inc. in March 2001. In September 2001, Genzyme acquired Novazyme, and assumed Novazyme s contractual obligation to us.

Interest income for the year ended December 31, 2002 was $1,108,000, compared to $3,704,000 for the corresponding period in 2001. The decrease was due to lower average cash and cash equivalents and marketable securities balances, as well as lower interest rates, during 2002.

Interest expense for the year ended December 31, 2002 was zero, compared to $188,000 for the corresponding period in 2001. The decrease was due to the fact that in 2002 we capitalized $150,000 of interest expense on our two capital construction projects, as discussed in the Liquidity and Capital Resources section of this MD&A. In accordance with GAAP, we recognized capitalized interest for these projects only to the extent of our actual interest expense, resulting in no reported interest expense for 2002.

**Recent Accounting Pronouncements**

In April 2003, the Financial Accounting Standards Board (FASB) issued Statement of Financial Accounting Standards No. 149, Amendment of Statement 133 on Derivative Instruments and Hedging Activities (SFAS No. 149). This Statement amends and clarifies accounting for derivative instruments, including certain derivative instruments embedded in other contracts, and for hedging activities under SFAS No. 133. SFAS No. 149 was effective for contracts entered into or modified after June 30, 2003, for hedging relationships designated after June 30, 2003, and to certain preexisting contracts. The adoption of SFAS No. 149 did not have a material impact on our financial statements.

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In May 2003, the FASB issued SFAS No. 150, Accounting for Certain Financial Instruments with Characteristics of both Liabilities and Equity . This Statement establishes standards for how an issuer classifies and measures certain financial instruments with characteristics of both liabilities and equity. SFAS No. 150 was effective for financial instruments entered into or modified after May 31, 2003, and is otherwise effective July 1, 2003. The adoption of SFAS No. 150 did not have an impact on our financial statements as we do not have any instruments that are within the scope of this statement.

In December 2003, the FASB issued FASB Interpretation No. 46 (revised December 2003), Consolidation of Variable Interest Entities (FIN 46R), which addresses how a business enterprise should evaluate whether it has a controlling financial interest in an entity through means other than voting rights and accordingly should consolidate the entity. FIN 46R replaces FASB Interpretation No. 46, Consolidation of Variable Interest Entities, which was issued in January 2003. We will be required to apply FIN 46R to variable interests in variable interest entities created after December 31, 2003. We do not have any variable interests in variable interest entities.

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## FACTORS AFFECTING THE COMPANY S PROSPECTS

### *Risks Related to Development-Stage Company*

***If we fail to obtain necessary funds for our operations, we will be unable to maintain and improve our technology position and we will be unable to develop and commercialize our therapeutic proteins.***

To date, we have funded our operations primarily through proceeds from the public and private placements of equity securities. We have also funded our operations to a lesser extent from proceeds from property and equipment financing, interest earned on investments, revenues from corporate collaborations and gains from the sale of investments. We believe that our existing cash and short-term investments, expected revenue from collaborations and license arrangements, anticipated financing of capital expenditures, and interest income should be sufficient to meet our operating and capital requirements into 2005. Our present and future capital requirements depend on many factors, including:

- the level of research and development investment required to develop our therapeutic proteins and improve our technology position;
- the progress of preclinical and clinical testing, which can be unpredictable in drug development;
- the cost of obtaining or manufacturing protein;
- the time and cost involved in obtaining regulatory approvals;
- our ability and willingness to enter into new agreements with collaborators and to extend our existing collaborations, and the terms of these agreements;
- our success rate or that of our collaborators in preclinical and clinical efforts associated with milestones and royalties;
- the timing, willingness, and ability of our collaborators to commercialize products incorporating our technologies;
- the costs of recruiting and retaining qualified personnel;
- the costs of filing, prosecuting, defending, and enforcing patent claims and other intellectual property rights;
- our need or decision to acquire or license complementary technologies or new drug targets; and
- changes in product candidate development plans that may be needed to address any difficulties in clinical studies or during commercialization.

We will require significant amounts of additional capital in the future, and we do not have any assurance that funding will be available when we need it on terms that we find favorable, if at all. We may seek to raise these funds through public or private equity offerings, debt financings, credit facilities, or through corporate collaborations and licensing arrangements.

If we raise additional capital by issuing equity securities, our existing stockholders percentage ownership will be reduced and they may experience substantial dilution. We may also issue equity securities that provide for rights, preferences, or privileges senior to those of our common stock. If we raise additional funds by issuing debt securities, these debt securities would have rights, preferences, and privileges senior to those of our common stock, and the terms of the debt securities issued could impose significant restrictions on our operations. If we enter into a credit facility, the agreement may require us to maintain compliance with financial covenants and restrict our ability to incur additional debt, pay dividends, make redemptions or repurchases of capital stock, make loans, investments

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or capital expenditures, or engage in other activities. If we raise additional funds through collaborations and licensing arrangements, we may be required to relinquish some rights to our technologies or drug candidates, or to grant licenses on terms that are not favorable to us. If adequate funds are not available or are not available on acceptable terms, our ability to fund our operations, take advantage of opportunities, develop products or technologies, or otherwise respond to competitive pressures could be significantly delayed or limited, and we may need to downsize or halt our operations.

***We have a history of losses, and we may incur continued losses for some time.***

We have incurred losses each year, including net losses of $13.3 million for the year ended December 31, 2001, $26.4 million for the year ended December 31, 2002, and $37.7 million for the year ended December 31, 2003. Given our planned level of operating expenses, we expect to continue incurring losses for some time. As of December 31, 2003, we had an accumulated deficit of $145.7 million. To date, we have derived substantially all of our revenue from corporate collaborations, license agreements, and investments. We expect that substantially all of our revenue for the foreseeable future will result from these sources and from the licensing of our technologies. We also expect to spend significant amounts to expand our research and development on our proprietary drug candidates and technologies, maintain and expand our intellectual property position, expand our manufacturing scale-up activities, and expand our business development and commercialization efforts. We may continue to incur substantial losses even if our revenues increase.

In 2004, we expect our investment in capital expenditures to be approximately $10.0 million. In addition to the credit agreement we entered into in January 2004, we may finance some or all of these capital expenditures through capital leases or the issuance of new debt or equity. Our level of operating expenditures will vary depending upon the stage of development of our proprietary proteins and the number and nature of collaboration agreements into which we enter.

***We have not yet commercialized any products or technologies, and we may never become profitable.***

We have not yet developed any products or commercialized any products or technologies, and we may never be able to do so. Since we began operations in 1990, we have not generated any revenues, except for interest income and revenues from collaborative agreements and investments. We do not know when or if we will complete any of our product development efforts, receive regulatory approval for any of our product candidates, or successfully commercialize any approved products. Even if we are successful in developing products that are approved for marketing, we will not be successful unless our products, and products incorporating our technologies, gain market acceptance. The degree of market acceptance of these products will depend on a number of factors, including:

- the receipt of regulatory approvals in the countries, and for the uses, we seek;
- the establishment and demonstration in the medical community of the safety and clinical efficacy of our products and their potential advantages over existing therapeutic products;
- the adequacy and success of distribution, sales and marketing efforts; and
- pricing and reimbursement policies of government and third-party payors, such as insurance companies, health maintenance organizations and other plan administrators.

Physicians, patients, payors or the medical community in general may be unwilling to accept, utilize or recommend any of our products or products incorporating our technologies. As a result, we are unable to predict the extent of future losses or the time required to achieve profitability, if at all. Even if we or our collaborators successfully develop one or more products that incorporate our technologies, we may not become profitable.

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***Risks Related to Development of Products and Technologies***

***We have limited product development and manufacturing experience, and we may be unable to develop therapeutic proteins and commercialize our technologies.***

Until recently, we have not focused on the development of our own proprietary products. We are now seeking to use our GlycoAdvance and GlycoPEGylation technologies to develop proprietary next-generation proteins, generally in collaboration with a partner. Our technologies may not result in the successful modification, optimization or development of proteins that are safe or efficacious. Because the development of new pharmaceutical products is highly uncertain, our technologies may not produce any commercially successful proteins. If we fail to successfully obtain protein supplies on reasonable terms or modify the proteins we select for development, we will not be able to commercialize our next-generation drug candidates, and our customers may not be able to develop drug candidates incorporating our technologies.

To date, we have manufactured only small quantities of our enzymes, sugar nucleotides and other reagents. We intend to manufacture these reagents for use in our proprietary product development programs and for use by our collaborators. Our success depends on our ability to manufacture these compounds on a commercial scale, at reasonable cost, and in accordance with current Good Manufacturing Practices, or cGMP, prescribed by the U.S. Food and Drug Administration, or FDA. We may not be able to manufacture sufficient quantities of the products we develop, even to meet our needs for pre-clinical or clinical development, and we may have problems complying, or maintaining compliance, with cGMP.

In addition to the normal scale-up risks associated with any manufacturing process, we may face unanticipated problems unique to the manufacture of enzymes, sugar nucleotides, other reagents, or proteins. If we are unable to develop commercial-scale manufacturing capacity, we would seek collaborators, licensees, or contract manufacturers to manufacture the compounds necessary to commercialize our technologies. We may not be able to find parties willing and able to manufacture these compounds at acceptable prices.

Any manufacturing facility must adhere to the FDA s evolving regulations on cGMP, which are enforced by the FDA through its facilities inspection program. The manufacture of products at any facility will be subject to strict quality control, testing, and record keeping requirements, and continuing obligations regarding the submission of safety reports and other post-market information. Ultimately, we or our contract manufacturers may not meet these requirements.

If we encounter delays or difficulties in connection with manufacturing, commercialization of our products and technologies could be delayed, or we could breach our obligations under our collaborative agreements.

***Our success depends on our ability, and the ability of our partners, to meet the challenges of protein drug development.***

The development of protein drugs involves a range of special challenges at various stages of the process. In the preclinical phase of product development, we and our partners will face several potential problems, including obtaining supplies of the recombinant protein on commercially reasonable terms, successfully remodeling the native protein using our GlycoAdvance and GlycoPEGylation technologies, and achieving adequate yields of the next-generation protein. We also may have to address difficult issues, such as protein refolding problems and contamination, which could delay or stop our progress.

If we cannot obtain native proteins or do not succeed in developing and scaling up our processes to enable the production of sufficient supplies of protein for large clinical trials or commercialization, in each case, at a commercially reasonable cost and on schedule, our programs could be significantly delayed or discontinued. Product candidates that appear promising in the early phases of development may fail in clinical trials for several reasons, such as results indicating that the product candidate is less effective than desired (e.g., the trial failed to meet its primary objectives) or that it has harmful or problematic side effects. Even if clinical trials are successful, problems can arise later during commercialization. We are aware that one marketed EPO product was associated with pure red cell aplasia in post-marketing surveillance studies. This highlights the fact that even after a product is approved for marketing, problems may arise which can negatively affect sales and increase costs.

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Our failure to solve any of these problems could delay or prevent the commercialization of products incorporating our technologies and could negatively impact our business.

***Our success depends on the success of our collaborative relationships and the success of our collaborators.***

We will be relying to a large extent on collaborative partners to co-develop our products and to commercialize products made using our technologies. We do not anticipate continuing the development of our proprietary drug candidates beyond early Phase II studies unless we have a corporate partner. We anticipate that substantially all of our revenues during the next several years will continue to be generated from collaboration or license agreements. Our partnering strategy entails many risks, including:

- we may be unsuccessful in entering into collaborative agreements for the co-development of our products or the commercialization of products incorporating our technologies;
- we may not be successful in adapting our technologies to the needs of our collaborative partners;
- our collaborators may not be successful in, or may not remain committed to, co-developing our products or commercializing products incorporating our technologies;
- our collaborators may not commit sufficient resources to incorporating our technologies into their products;
- our collaborators may seek to develop other proprietary alternatives to our products or technologies;
- our collaborators are not obligated to market or commercialize our products or products incorporating our technologies, and they are not required to achieve any specific commercialization schedule;
- our collaborative agreements are generally terminable by our partners on short notice; and
- continued consolidation in our target markets may limit our ability to enter into collaboration agreements, or may result in terminations of existing collaborations.

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

Any of our present or future collaborators may breach or terminate their agreements with us or otherwise fail to conduct their collaborative activities successfully and in a timely manner. In addition, we may dispute the application of payment provisions under any of our collaborative agreements. If any of these events occur or if we fail to enter into or maintain collaborative agreements, we may not be able to commercialize our products and technologies, and our prospects would be significantly harmed.

***We may be exposed to product liability and related risks.***

The use in humans of compounds developed by us or incorporating our technologies may result in product liability claims. Product liability claims can be expensive to defend, and may result in large settlements of claims or judgments against us. Even if a product liability claim is not successful, the adverse publicity, time, and expense involved in defending such a claim may interfere with our business. We may not be able to obtain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses.

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***Risks Related to Intellectual Property***

***Infringing the patents of others could result in litigation and delay development of our proprietary products. The failure to obtain or maintain adequate patents, and other intellectual property protection, could impact our ability to compete effectively.***

Our commercial success depends in part on avoiding infringing patents and proprietary rights of third parties. As we seek to develop next-generation proprietary products, we will have to investigate the patent protection for our target proteins. There have been significant litigation and interference proceedings regarding patent rights, and the patent situation regarding particular products is often complex and uncertain. For example, with respect to EPO, the target of our first development program, the status of issued patents is currently being litigated and may delay our ability to market an improved EPO in the U.S. As we choose other targets, we may face uncertainty and litigation could result, which could lead to liability for damages, prevent our development and commercialization efforts, and divert resources from our business strategy. It is possible that we will not be aware of pending patent applications that are relevant to our product candidates, either because our searches do not find them or because they are not yet publicly available.

The cost of any litigation challenging our right to pursue our target proteins or technologies could be substantial. Others seeking to develop next-generation versions of proteins, or the holders of patents on our target proteins, may have greater financial resources, making them better able to bear the cost of litigation. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to develop, manufacture, and market products, form strategic alliances, and compete in the marketplace.

***The failure to obtain, maintain or protect patents and other intellectual property could impact our ability to compete effectively.***

To compete effectively, we need to develop and maintain a proprietary position with regard to our own technologies, products and business. Legal standards relating to the validity and scope of claims in our technology field are still evolving. Therefore, the degree of future protection for our proprietary rights in our core technologies and products made using these technologies is also uncertain. The risks and uncertainties that we face with respect to our patents and other proprietary rights include the following:

- the pending patent applications we have filed or to which we have exclusive rights may not result in issued patents or may take longer than we expect to result in issued patents;
- we may be subject to interference proceedings;
- we may be subject to opposition proceedings in foreign countries;
- the claims of any patents that are issued may not provide meaningful protection;
- we may not be able to develop additional proprietary technologies that are patentable;
- the patents licensed or issued to us or our customers may not provide a competitive advantage;

other companies may challenge patents licensed or issued to us or our customers;

other companies may independently develop similar or alternative technologies, or duplicate our technologies;

other companies may design around technologies we have licensed or developed; and

enforcement of patents is complex, uncertain and expensive.

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We cannot be certain that patents will be issued as a result of any of our pending applications, and we cannot be certain that any of our issued patents will give us adequate protection from competing products. For example, issued patents may be circumvented or challenged, declared invalid or unenforceable, or narrowed in scope. In addition, since publication of discoveries in the scientific or patent literature often lags behind actual discoveries, we cannot be certain that we were the first to make our inventions or to file patent applications covering those inventions. In the event that another party has also filed a patent application relating to an invention claimed by us, we may be required to participate in an interference proceeding declared by the U.S. Patent and Trademark Office to determine priority of invention, which could result in substantial uncertainties and cost for us, even if the eventual outcome were favorable to us. It is also possible that others may obtain issued patents that could prevent us from commercializing our products or require us to obtain licenses requiring the payment of significant fees or royalties in order to enable us to conduct our business. As to those patents that we have licensed, our rights depend on maintaining our obligations to the licensor under the applicable license agreement, and we may be unable to do so.

The cost to us of any patent litigation or other proceeding relating to our patents or applications, even if resolved in our favor, could be substantial. Our ability to enforce our patent protection could be limited by our financial resources, and may be subject to lengthy delays. If we are unable to effectively enforce our proprietary rights, or if we are found to infringe the rights of others, we may be in breach of our license agreements with our partners.

Third parties from time to time may assert that we are infringing their patents, trade secrets or know-how. In addition, future patents may issue 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 or our partners ability to further develop or commercialize some or all of our products or technologies in the U.S. and abroad, and could result in the award of substantial damages. If we are found to infringe, we may be required to obtain one or more licenses from third parties. There can be no assurance that 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.

In addition to patents and patent applications, we depend upon trade secrets and proprietary know-how to protect our proprietary technology. We require our employees, consultants, advisors, and collaborators to enter into confidentiality agreements that prohibit the disclosure of confidential information to any other parties. We require our employees and consultants to disclose and assign to us their ideas, developments, discoveries, and inventions. These agreements may not, however, provide adequate protection for our trade secrets, know-how, or other proprietary information in the event of any unauthorized use or disclosure.

***International patent protection is uncertain.***

Patent law outside the U.S. is uncertain, and is currently undergoing review and revision in many countries. In addition, the laws of some foreign countries may not protect our intellectual property rights to the same extent as U.S. laws. We may participate in opposition proceedings to determine the validity of foreign patents belonging to us or our competitors, which proceedings could result in substantial costs and diversion of our efforts. Finally, some of our patent protection in the U.S. is not available to us in foreign countries due to the differences in the patent laws of those countries.

***We may have to develop or license alternative technologies if we are unable to maintain or obtain key technology from third parties.***

We have licensed patents and patent applications from a number of institutions. Some of our proprietary rights have been licensed to us under agreements that have performance requirements or other contingencies. The failure to comply with these provisions could lead to termination or

modifications of our rights to these licenses. Additionally, we may need to obtain additional licenses to patents or other proprietary rights from other parties to facilitate development of our proprietary technology base. If our existing licenses are terminated or if we are unable to obtain such additional licenses on acceptable terms, our ability to perform our own research and development and to comply with our obligations under our collaborative agreements may be delayed while we seek to develop or license alternative technologies.

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***Risks Related to Competition***

***If our competitors succeed in developing more effective or less costly products, we will may not be able to commercialize any next-generation protein therapeutics.***

Our business is characterized by extensive research efforts and rapid technological progress. New developments in molecular biology, medicinal chemistry, and other fields of biology and chemistry are expected to continue at a rapid pace in both industry and academia. Our potential competitors include both public and private pharmaceutical and biotechnology companies, as well as academic institutions, governmental agencies and other public and private research organizations which are also conducting research activities and seeking patent protection.

A number of these competitors are working on the development of next-generation protein therapeutics. Some of these competitors include Maxygen, Applied Molecular Evolution, Nektar, Enzon, Human Genome Sciences, BioRexis and Alkermes. Other companies have programs focused on developing next-generation or improved versions of EPO and G-CSF, and some are already marketing improved versions of these products. These companies include Amgen, Gryphon, Transkaryotic Therapeutics, Human Genome Sciences, ARIAD and Affymax. Other companies are active in this area, and we expect that competition will increase.

There are several companies that are engaged in glycobiology research. These companies include Crucell, GLYCART, GlycoFi and Momenta.

Compared to us, many of these companies have more:

- financial, scientific, and technical resources;
- product development, manufacturing and marketing capabilities;
- experience conducting preclinical studies and clinical trials of new products; and
- experience in obtaining regulatory approvals for products.

Competitors may succeed in developing products and technologies that are more effective and less costly than ours and that would render our products or technologies, or both, obsolete or noncompetitive. We know that other companies with substantial resources are working on the development of next-generation proteins, and they may achieve better results in remodeling our target proteins or the target proteins of our potential collaborators.

Competitors also may prove to be more successful in designing, manufacturing and marketing products. If we are successful in developing our own drug candidates or versions of drugs that are no longer patented, we will compete with other drug manufacturers for market share. If we are unable to compete successfully, our commercial opportunities will be diminished.

In addition, while there is no abbreviated regulatory pathway for follow-on biologics, this possibility is under discussion in the U.S. and other jurisdictions. If an abbreviated regulatory process is adopted for the approval of follow-on biologics in any major market, competition could increase in related segments of the therapeutic protein market.

***We may be unable to retain key employees or recruit additional qualified personnel.***

Because of the specialized scientific nature of our business, we are highly dependent upon qualified scientific, technical and managerial personnel, including our research and development team and our president and CEO, C. Boyd Clarke. The development of our business is dependent upon our management team s ability to evaluate collaboration opportunities and on our CEO s ability to focus the Company s efforts. Our anticipated research and development efforts will require additional expertise and the addition of new qualified personnel. There is intense competition for qualified management and research and development personnel in the pharmaceutical field. Therefore, we may not be able to attract and retain the qualified personnel necessary for the development of our business. The loss of the services of existing personnel, as well as the failure to recruit additional key scientific,

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technical and managerial personnel in a timely manner, would harm our research and development programs, our ability to manage day-to-day operations, attract collaboration partners, attract and retain other employees, and generate revenues. We do not maintain key man life insurance on any of our employees.

***Risks Related to Government Regulation***

***We are subject to extensive government regulation, and we or our collaborators may not obtain necessary regulatory approvals.***

The research, development, manufacture and control, marketing, and sale of our reagents and product candidates manufactured using our technologies are subject to significant, but varying, degrees of regulation by a number of government authorities in the U.S. and other countries.

Pharmaceutical product candidates manufactured using our technologies must undergo an extensive regulatory approval process before commercialization. This process is regulated by the FDA and by comparable agencies in the EU and other countries. The U.S. and foreign regulatory agencies have substantial discretion to terminate clinical trials, require additional testing, delay or withhold registration and marketing approval, and mandate product withdrawals. The specific risks of protein drugs may result in the application of more stringent regulatory requirements prior to approval of our product candidates. Even if regulatory approvals were obtained, our manufacturing processes would be subject to continued review by the FDA and other regulatory authorities. Any later discovery of unknown problems with our products, products incorporating our technologies, or manufacturing processes could result in restrictions on such products or manufacturing processes, including potential withdrawal of the products from the market. In addition, if regulatory authorities determine that we have not complied with regulations in the research and development of a product candidate or the manufacture and control of our reagents, then we may not obtain necessary approvals to market and sell the product candidate or reagents.

Neither we nor our collaborators have submitted any product candidates incorporating our technologies for approval to the FDA or any other regulatory authority. If any product candidate manufactured using our technology is submitted for regulatory approval, it may not receive the approvals necessary for commercialization, the desired labeling claims, or adequate levels of reimbursement. Any delay in receiving, or failure to receive, these approvals would adversely affect our ability to generate product revenues or royalties. In addition, new governmental regulations may delay or alter regulatory approval of any product candidate manufactured using our technology, and could affect competition by making market entry easier for manufacturers of follow-on biologics. We cannot predict the impact of adverse governmental action that might arise from future legislative and administrative action.

***Third-party reimbursement for our collaborators or our future product candidates may not be adequate.***

Even if regulatory approval is obtained to sell any product candidates incorporating our technologies, our future revenues, profitability, and access to capital will be determined in part by the price at which we or our collaborators can sell such products. There are continuing efforts by governmental and private third-party payors to contain or reduce the costs of health care through various means. We expect a number of federal, state, and foreign proposals to control the cost of drugs through governmental regulation. We are unsure of the form that any health care reform legislation may take or what actions federal, state, foreign, and private payors may take in response to the proposed reforms. Therefore, we cannot predict the effect of any implemented reform on our business.

Our ability to commercialize our products successfully will depend, in part, on the extent to which reimbursement for the cost of such products and related treatments will be available from government health administration authorities, such as Medicare and Medicaid in the U.S., private health insurers, and other organizations. Significant uncertainty exists as to the reimbursement status of newly approved healthcare products, particularly for indications for which there is no current effective treatment or for which medical care typically is not sought. Adequate third-party coverage may not be available to enable us to maintain price levels sufficient to realize an appropriate return on investment in product research and development. Inadequate coverage and reimbursement levels provided by government and third-party payors for use of our or our collaborators products may cause these products to fail to achieve market acceptance and would cause us to lose anticipated revenues and delay achievement of profitability.

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***Risks Related to Facilities, Business Interruption, and the Environment***

***The use of hazardous materials in our operations may subject us to environmental claims or liability.***

Our research and development processes involve the controlled use of hazardous materials, chemicals, and radioactive compounds. We conduct experiments that are quite common in the biotechnology industry, in which we use small quantities of chemical hazards, including those that are corrosive, toxic and flammable, and trace amounts of radioactive materials. The risk of accidental injury or contamination from these materials cannot be entirely eliminated. We do not maintain a separate insurance policy for these types of risks. In the event of an accident or environmental discharge, we may be held liable for any resulting damages, and any liability could exceed our resources. We are subject to federal, state, and local laws and regulations governing the use, storage, handling, and disposal of these materials and specified waste products. The cost of compliance with these laws and regulations could be significant.

***Destructive actions by activists or terrorists could damage our facilities, interfere with our research activities, and cause ecological harm.***

Activists and terrorists have shown a willingness to injure people and damage physical facilities, equipment and biological materials to publicize or otherwise further their ideological causes. Our operations and research activities, and services conducted for us by third parties, could be adversely affected by such acts. Any such damage could delay our research projects and decrease our ability to conduct future research and development. Damage caused by activist or terrorist incidents could also cause the release of hazardous materials, including chemicals, radioactive and biological materials, which could be costly to remediate and damaging to our reputation.

Any significant interruption to our ability to conduct our business operations, research and development activities, or manufacturing operations could reduce our revenue and increase our expenses.

***Risks Related to Stock Market***

***Our stock price may continue to experience fluctuations.***

The market prices of securities of thinly traded biotechnology companies, such as ours, generally are highly volatile. For example, in the past 24 months, the price of our common stock reached a low of $5.90 per share in October, 2002, and a high of $35.35 per share in February, 2002. During the past 12 months the price of our common stock has traded as low as $6.03 per share in February, 2003, and as high as $13.80 per share in January, 2004.

In this market environment, the sale of a substantial number of shares of our common stock in the public market or the perception that such a sale might occur would likely have an adverse effect on the market price of our common stock, at least for the short term. We have a number of investors who hold relatively large positions in our securities. A decision by any of these investors to sell all or a block of their holdings of our common stock could cause our stock price to drop significantly.

The market also continues to experience significant price and volume fluctuations, some of which are unrelated to the operating performance of particular companies. In recent years, the price of our common stock has fluctuated significantly and may continue to do so in the future. Many factors could have a significant effect on the market price of our common stock, including:

- preclinical and clinical trial results,
- product development delays,
- an announcement or termination of a collaborative relationship by us or any of our partners or competitors,
- developments relating to our patent position or other proprietary rights,

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announcements of technological innovations or new therapeutic products,

government regulations,

public concern as to the safety of products 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.

If we raise additional capital by issuing equity securities in a fluctuating market, many or all of our existing stockholders may experience substantial dilution, and if we need to raise capital by issuing equity securities at a time when our stock price is down, we may have difficulty raising sufficient capital to meet our requirements. If any of the risks described in these Factors Affecting the Company s Prospects occurred, or if any unforeseen risk affected our performance, it could have a dramatic and adverse impact on the market price of our common stock.

***Foreign Exchange Risks***

***Changes in foreign currency exchange rates could result in increased costs.***

We have entered into agreements denominated in Euros, and, in the future, we may enter into agreements denominated in Euros or other foreign currencies. To date, we have not entered into any contracts to reduce the risk of fluctuations in currency exchange rates. In the future, depending upon the amounts payable under any such agreements, we may enter into forward foreign exchange contracts to reduce the risk of unpredictable changes in these costs. However, due to the variability of timing and amount of payments under any such agreements, foreign exchange contracts may not mitigate the potential adverse impact on our financial results.

**ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURE ABOUT MARKET RISK.**

Our holdings of financial instruments are comprised primarily of government agency securities. All such instruments are classified as securities held to maturity. We seek reasonable assuredness of the safety of principal and market liquidity by investing in rated fixed income securities, while at the same time seeking to achieve a favorable rate of return. Our market risk exposure consists principally of exposure to changes in interest rates. Our holdings are also exposed to the risks of changes in the credit quality of issuers. We typically invest in the shorter-end of the maturity spectrum. As of December 31, 2003, the marketable securities that we held consisted of obligations of U.S government agencies. The approximate principal amount and weighted-average interest rate per year of our investment portfolio as of December 31, 2003 was approximately $53,060,000 and 1.3%, respectively.

The interest rates on our taxable and tax-exempt bonds, the value of which was $3,900,000 at December 31, 2003, vary weekly, depending on the market rates for AA-rated taxable and tax-exempt obligations. We are currently not engaged in hedging activities. As of December 31, 2003,

the weighted-average, effective interest rate was approximately 2.7% per year.

**ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA.**

**(a) Financial Statements.**

The Financial Statements required by this item are attached to this Annual Report on Form 10-K beginning on page F-1.

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**(b) Supplementary Data.**

Quarterly financial data (unaudited)

(in thousands, except per share data)

| 2003 Quarter Ended | Dec. 31 | Sept. 30 | June 30 | Mar. 31 |
|---|---|---|---|---|
| Revenue from collaborative agreements | $ 564 | $ 150 | $ 651 | $ 70 |
| Net loss | (9,696) | (10,338) | (9,226) | (8,421) |
| Basic and diluted net loss per share(1) | (0.49) | (0.59) | (0.54) | (0.53) |

| 2002 Quarter Ended | Dec. 31 | Sept. 30 | June 30 | Mar. 31 |
|---|---|---|---|---|
| Revenue from collaborative agreements | $ 294 | $ 2,187 | $ 1,561 | $ 771 |
| Net loss | (6,377) | (5,955) | (6,490) | (7,595) |
| Basic and diluted net loss per share | (0.45) | (0.42) | (0.45) | (0.53) |

(1) The sum of quarterly loss per share may differ from the full-year amount due to changes in the number of shares outstanding during the year.

**ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE.**

As previously reported on a Current Report on Form 8-K dated April 29, 2002 (the Form 8-K ), our Board of Directors, upon recommendation of the Audit Committee, informed the Company s independent public accountants, Arthur Andersen LLP ( Arthur Andersen ), that they would be dismissed as the Company s independent public accountants and engaged KPMG LLP ( KPMG ) to serve as the Company s independent public accountants for the fiscal year 2002. The appointment of KPMG was effective immediately.

**ITEM 9A. CONTROLS AND PROCEDURES.**

We carried out an evaluation, under the supervision and with the participation of our management, including our principal executive officer and principal financial officer, of the effectiveness of the design and operation of our disclosure controls and procedures as such term is defined under Rule 13a-15(e) promulgated under the Securities Exchange Act of 1934, as amended (the Exchange Act ), for financial reporting as of December 31, 2003. Based on that evaluation, our principal executive officer and principal financial officer concluded that these controls and procedures are effective to ensure that information required to be disclosed by the Company in reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported as specified in Securities and Exchange Commission rules and forms. There were no changes in these controls or procedures identified in connection with the evaluation of such controls or procedures that occurred during our last fiscal quarter, or in other factors that have materially affected, or are reasonably likely to materially affect, these controls or procedures.

Our disclosure controls and procedures are designed to ensure that information required to be disclosed by us in the reports that we file or submit under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the rules and forms of the Securities and Exchange Commission. These disclosure controls and procedures include, among other things, controls and procedures designed to ensure that information required to be disclosed by us in the reports that we file under the Exchange Act is accumulated and communicated to our management, including our principal executive officer and principal financial officer, as appropriate to allow timely decisions regarding required disclosure. Our internal controls and procedures for financial reporting are designed to provide reasonable assurance, and management believes that they provide such

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reasonable assurance, that our transactions are properly authorized, our assets are safeguarded against unauthorized or improper use, and our transactions are properly recorded and reported, in order to permit the preparation of our financial statements in conformity with generally accepted accounting principles.

Our management group, including our principal executive officer and principal financial officer, does not expect that our disclosure controls and internal controls and related procedures will prevent all error and all fraud. A control system, no matter how well designed and implemented, can provide only reasonable assurance that the objectives of the control system are met. In addition, the design and implementation of a control system must reflect the fact that there are resource constraints, and the benefits of controls must be considered in relation to their costs. The design of any system of controls is based, in part, upon certain assumptions about the likelihood of future events, which may prove to be incorrect. Due to the limitations of all control systems, no evaluation of controls can provide absolute assurance that all control issues and instances of fraud, if any, within an organization have been detected or prevented.

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## PART III

### ITEM 10. DIRECTORS AND EXECUTIVE OFFICERS OF THE REGISTRANT.

The following table shows the name, age and position of each of our directors as of February 15, 2004:

| Name of Director | Age | Position |
|---|---|---|
| C. Boyd Clarke | 55 | Chairman |
| Brian H. Dovey | 62 | Director |
| L. Patrick Gage, Ph.D. | 61 | Director |
| William F. Hamilton, Ph.D. | 64 | Director |
| Douglas J. MacMaster, Jr. | 73 | Director |
| Mark H. Rachesky, M.D. | 44 | Director |
| Stephen A. Roth, Ph.D. | 61 | Director |
| Lowell E. Sears | 52 | Director |
| Elizabeth H.S.Wyatt | 56 | Director |

**Biographic Information Regarding Our Directors as of February 15, 2004**

**C. Boyd Clarke**, 55, has served on our Board, and as President and Chief Executive Officer, since March 2002, and became Chairman of our Board in May 2003. From December 1999 through March 2002, Mr. Clarke was President and Chief Executive Officer of Aviron, a biotechnology company developing vaccines, which was acquired by MedImmune, and was also Chairman from January 2001 through March 2002. From 1998 through 1999, Mr. Clarke was Chief Executive Officer and President of U.S. Bioscience, Inc., a biotechnology company focused on products to treat cancer, which also was acquired by MedImmune. Mr. Clarke served as President and Chief Operating Officer of U.S. Bioscience, Inc. from 1996 to 1998. From 1977 to 1996, Mr. Clarke held a number of positions at Merck & Co., Inc., including being the first President of Pasteur-Merieux MSD, and most recently as Vice President of Merck Vaccines. Mr. Clarke serves as a director of QLT Inc., a global pharmaceutical company, and the Biotechnology Industry Organization. Mr. Clarke has a B.S. in biochemistry, and an M.A. in history from the University of Calgary. Mr. Clarke also serves on the Board of Trustees to the Textile Museum in Washington, D.C.

**Brian H. Dovey**, 62, has served on our Board since May 2003. He is a Managing Member of Domain Associates, L.L.C., a private venture capital management firm focused on life sciences, and has served in this capacity with the firm since 1988. He has served as Chairman of three companies and on the Board of Directors of some 20 additional companies, including Align Technology, Inc. and Cardiac Science, Inc. Prior to joining Domain, Mr. Dovey spent six years at Rorer Group, Inc. (now Aventis) and as President (1986 to 1988) was the primary architect of this Fortune 500 company s strategic shift to pharmaceuticals resulting in a doubling of annual sales to approximately $1 billion. Previously, he was President of Survival Technology, Inc., a start-up medical products company whose sales growth placed it in the top ten of the Inc 100. He also held management positions with Howmedica, Inc., Howmet Corporation, and New York Telephone. Mr. Dovey has served as both President and Chairman of the National Venture Capital Association and is on the Board of Trustees of the Wistar Institute and the Burnham Institute. Mr. Dovey received his B.A. from Colgate University and an M.B.A. degree from the Harvard Business School.

**L. Patrick Gage**, Ph.D., 61, has served on our Board since October 2002. Dr. Gage is Chairman of Compound Therapeutics, a private biotechnology company, and Chairman of the Dublin (IE) Molecular Medicine Centre. Dr. Gage has been appointed Venture Partner at Flagship Ventures and is an advisor to Perkin Elmer, Inc. and Warburg Pincus LLC. Dr. Gage served as Senior Vice President, Science and Technology,

at Wyeth, from 2001 to 2002, and as President of Wyeth Research from 1998 to 2002. Prior to Wyeth, Dr. Gage held positions of increasing responsibility at Genetics Institute, Inc. from 1989 to 1998, culminating with his service as President after the company was acquired by Wyeth. He also spent 18 years at Hoffmann-La Roche, Inc. in various scientific and management positions. Dr. Gage serves as a director of Protein Design Labs, Inc., a company focused on the discovery and development of humanized monoclonal antibodies for the treatment of disease. He is also a director of the Biotechnology Institute and the Philadelphia Orchestra Association. Dr. Gage has a B.S. in physics from Massachusetts Institute of Technology and a Ph.D. from The University of Chicago.

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**William F. Hamilton**, Ph.D., 64, has served on our Board since 1991. Dr. Hamilton has served on the University of Pennsylvania faculty since 1967, and is the Landau Professor of Management and Technology, and Director of the Jerome Fisher Program in Management and Technology at The Wharton School and the School of Engineering and Applied Science. He serves as a director of NovaDel Pharmaceuticals, Inc., a healthcare company engaged in the development of novel drug delivery technologies. Dr. Hamilton received his B.S. and M.S. in chemical engineering and his M.B.A. from the University of Pennsylvania, and his Ph.D. in applied economics from the London School of Economics.

**Douglas J. MacMaster, Jr.**, 73, has served on our Board since 1993. Mr. MacMaster served as Senior Vice President of Merck & Co., Inc. from 1988 to 1992, where he was responsible for worldwide chemical and pharmaceutical manufacturing, the Agvet Division, and the Specialty Chemicals Group. From 1985 to 1988, Mr. MacMaster was President of the Merck Sharp Dohme Division of Merck. Mr. MacMaster serves as a director of the following publicly-held companies: Stratton Mutual Funds, and Martek Biosciences Corp., a biological products manufacturing company. He received his B.A. from St. Francis Xavier University, and his J.D. from Boston College Law School.

**Mark H. Rachesky**, M.D., 44, has served on our Board since 1999. Dr. Rachesky is the founder and President of MHR Fund Management LLC and affiliates, investment managers of various private investment funds that invest in inefficient market sectors, including special situation equities and distressed investments. From 1990 through June 1996, Dr. Rachesky was employed by Carl C. Icahn, initially as a senior investment officer and for the last three years as sole Managing Director of Icahn Holding Corporation, and acting chief investment advisor. Dr. Rachesky is currently on the Board of Directors of Samsonite Corporation and Keryx Biopharmaceuticals, Inc. Dr. Rachesky is a graduate of Stanford University School of Medicine, and Stanford University School of Business. Dr. Rachesky graduated from the University of Pennsylvania with a major in Molecular Aspects of Cancer.

**Stephen A. Roth**, Ph.D., 61, has served on our Board since 1989, and was Chairman from 1994 until May 2003. Dr. Roth is President and Chief Executive Officer of Immune Control Inc. He co-founded Neose, served as Chief Executive Officer from August 1994 until March 2002, and now serves as a consultant. From 1992 until August 1994, he served as Senior Vice President, Research and Development and Chief Scientific Officer of Neose. Dr. Roth was on the faculty of the University of Pennsylvania from 1980 to 1994, and was Chairman of Biology from 1982 to 1987. Dr. Roth serves as a director of Chiral Quest. Dr. Roth received his A.B. in biology from The Johns Hopkins University, and his Ph.D. in developmental biology from the Case Western Reserve University. He completed his post-doctorate training in carbohydrate chemistry at The Johns Hopkins University.

**Lowell E. Sears**, 52, has served on our Board since 1994. He has been a private investor involved in portfolio management and life sciences venture capital since April 1994. From 1988 until April 1994, Mr. Sears was Chief Financial Officer of Amgen Inc., a pharmaceutical company, and from 1992 until 1994, he also served as Senior Vice President responsible for the Asia-Pacific region. Mr. Sears is a director of Peninsula Pharmaceuticals. Mr. Sears received his B.A. in economics from Claremont McKenna College, and his M.B.A. from Stanford University.

**Elizabeth H.S. Wyatt,** 56, has served on our Board since May 2002. From 1980 through December 2000, Ms. Wyatt held a variety of positions at Merck & Co., Inc., most recently as Merck s Vice President, Corporate Licensing, heading Merck s worldwide product and technology acquisition activities. Prior to joining Merck in 1980, Ms. Wyatt was a consultant and an academic administrator, responsible for the Harvard Business School s first formal marketing of its executive education programs. She currently serves on the Boards of Directors of MedImmune, Inc. and ARIAD Pharmaceuticals, and on the Board of Trustees of Randolph-Macon College. Ms. Wyatt received her B.A., magna cum laude, from Sweet Briar College, an M. Ed. in counseling psychology from Boston University, and an M.B.A. with honors from Harvard University.

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The following table shows the name, age and position of each of our executive officers as of February 15, 2004:

| Name of Executive Officer | Age | Position |
|---|---|---|
| C. Boyd Clarke | 55 | President and Chief Executive Officer |
| George J. Vergis, Ph.D. | 42 | Executive Vice President, Commercial and Clinical Development |
| Joseph J. Villafranca, Ph.D. | 59 | Executive Vice President, Development Operations |
| David A. Zopf, M.D. | 61 | Executive Vice President and Chief Scientific Officer |
| Robert I. Kriebel | 61 | Senior Vice President and Chief Financial Officer |
| Debra J. Poul, Esq. | 51 | Senior Vice President and General Counsel |
| A. Brian Davis | 37 | Vice President, Finance |
| Marjorie A. Hurley, Pharm.D. | 44 | Vice President, Regulatory Affairs and Project Management |

**Biographic Information Regarding Our Executive Officers as of February 15, 2004 (other than Mr. Clarke whose biography appears above, with the directors biographies)**

**George J. Vergis,** Ph.D., 42, was elected Executive Vice President, Commercial and Clinical Development on February 3, 2004, after serving as our Senior Vice President, Business and Commercial Development since December 2002. From July 2001 to December 2002, he served as our Vice President, Business and Commercial Development. From January 1996 to May 2001, Dr. Vergis served as Vice President, New Product Development and Commercialization at Knoll Pharmaceutical Company, a division of BASF Pharma, responsible for the commercial planning, product development, and marketing for the immunology franchise. Prior to this position, Dr. Vergis was responsible for managing the endocrine business for BASF Pharma s Knoll Pharmaceutical Division. Dr. Vergis has held a variety of clinical and medical marketing positions at Wyeth Pharmaceuticals and Warner-Lambert Parke-Davis. Dr. Vergis received his BA in biology and history from Princeton University, his Ph.D. in physiology from The Pennsylvania State University, and his M.B.A. from Columbia University.

**Joseph J. Villafranca,** Ph.D., 59, was elected Executive Vice President, Development Operations on February 3, 2004, after serving as our Senior Vice President, Pharmaceutical Development and Operations since October 2002. From 1992 to 2002, he held various positions at Bristol-Myers Squibb, serving most recently as Vice President of Biologics Strategy and Biopharmaceuticals Operations. Prior to Bristol-Myers, Dr. Villafranca spent 20 years at The Pennsylvania State University, including eight years as the Evan Pugh Professor of Chemistry. Dr. Villafranca earned a B.S. in chemistry from the State University of New York and a Ph.D. in biochemistry/chemistry from Purdue University. He completed his post-doctoral training in biophysics at the Institute for Cancer Research in Philadelphia.

**David A. Zopf,** M.D., 61, has served as our Executive Vice President since January 2002 and became Executive Vice President and Chief Scientific Officer on February 3, 2004. He served as our Vice President, Drug Development from 1992 to January 2002. From 1991 to 1992, we engaged Dr. Zopf as a consultant on the biomedical applications of complex carbohydrates. From 1988 to 1991, Dr. Zopf served as Vice President and Chief Operating Officer of BioCarb, Inc., a biotechnology company and the U.S. subsidiary of BioCarb AB, where he managed the research and development programs of novel carbohydrate-based diagnostics and therapeutics. Dr. Zopf received his A.B. in zoology from Washington University, and his M.D. from Washington University School of Medicine.

**Robert I. Kriebel,** 61, has served as our Senior Vice President and Chief Financial Officer since August 2002. From 1991 through 1999, he held various positions at U.S. Bioscience, Inc., most recently as Executive Vice President, Chief Financial Officer and Director. Prior to U.S. Bioscience, Mr. Kriebel held various positions with Rhone-Poulenc Rorer Inc. (formerly Rorer Group Inc.) from 1974 until November 1990. From 1987 to November 1990 he was Vice President and Controller of Armour Pharmaceutical Company, a subsidiary of Rorer Group Inc. In 1986, Mr. Kriebel was Vice President-Investor Relations of Rorer Group Inc. and from 1979 to 1985, he was Treasurer of Rorer Group Inc. Mr. Kriebel has a B.S. in economics from Roanoke College.

**Debra J. Poul,** Esq., 51, has served as our Senior Vice President, General Counsel since December 2002. From May 2002 to December 2002, she served as our Vice President and General Counsel, and from January 2000

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until May 2002, she served as our General Counsel. From January 1995 to January 2000, Ms. Poul was Of Counsel at Morgan Lewis. From September 1978 to December 1994, Ms. Poul was at Dechert, serving as Counsel from 1989 to 1994. Ms. Poul received her B.A. from the University of Pennsylvania and her J.D. from Villanova University.

**A. Brian Davis**, 37, has served as our Vice President, Finance since August 2002. From 1994 until August 2002, Mr. Davis served in a variety of positions, most recently as Acting Chief Financial Officer and Senior Director, Finance. From 1991 to 1994, Mr. Davis was employed by MICRO HealthSystems, Inc., a provider of healthcare information systems, where he served most recently as Corporate Controller. Mr. Davis is licensed as a Certified Public Accountant, received his B.S. in accounting from Trenton State College and his M.B.A. from the Wharton School of the University of Pennsylvania.

**Marjorie A. Hurley**, Pharm.D., 44**,** has served as Vice President, Regulatory Affairs and Project Management, since May 2002. She served as our Senior Director of Regulatory Affairs from January 2001 to May 2002, and as our Director of Regulatory Affairs from 1993 to May 2000. From 1987 to 1993, Dr. Hurley served in various positions, including Assistant Director of Regulatory Affairs, at Cytogen Corporation, a biotechnology company. From 1984 to 1987, she held several positions, including Project Coordinator, at the Wyeth-Ayerst Laboratories division of American Home Products Corp. (now Wyeth). Dr. Hurley received her B.S. in pharmacy and her Pharm.D. from the University of Michigan.

**Section 16(a) Beneficial Ownership Reporting Compliance**

Based solely upon a review of reports of stock ownership (and changes in stock ownership) and written representations received by us, we believe that our directors and executive officers met all of their filing requirements under Section 16(a) of the Securities and Exchange Act of 1934 during the year ended December 31, 2003, except for the late filing of one Form 4, which was made by Mr. MacMaster on April 24, 2003 in respect of his exercise of a stock option for cash on April 17, 2003.

**Audit Committee**

The Audit Committee consists of three directors, Lowell E. Sears (Chairman), Brian H. Dovey and William F. Hamilton, Ph.D., all of whom are independent as defined in our Corporate Governance Principles and under the rules of the Securities and Exchange Commission and NASDAQ. The Board of Directors has determined that Mr. Sears is an audit committee financial expert as defined in Item 401(h) of Regulation S-K. The Audit Committee operates pursuant to a charter, which can be viewed on our website at www.neose.com (under About Neose ).

**Code of Conduct**

We have a Code of Business Conduct and Ethics, which can be viewed on our website at www.neose.com (under About Neose ). We require all employees to adhere to this Code in addressing the legal and ethical issues encountered in conducting their work. The Code of Business Conduct and Ethics requires that our employees avoid conflicts of interest, comply with all laws and other legal requirements, conduct business in an honest and ethical manner, and otherwise act with integrity and in the Company s best interest. All of our employees were required to certify that they reviewed and understood this Code when they received it during 2003 or upon their later hire date, and again at the end of 2003. Our Code of Business Conduct and Ethics is intended to comply with Item 406 of the SEC s Regulation S-K and the rules of the Nasdaq stock market.

The Code of Business Conduct and Ethics includes procedures for reporting violations of the Code, which are applicable to all employees. The Sarbanes-Oxley Act of 2002 requires companies to have procedures to receive, retain and treat complaints received regarding accounting, internal accounting controls or auditing matters and to allow for the confidential and anonymous submission by employees of concerns regarding questionable accounting or auditing matters. The Code of Business Conduct and Ethics also includes these required procedures.

Any waiver or amendment of the Code of Business Conduct and Ethics for designated senior officers, including our chief executive officer and chief financial officer, will be disclosed promptly on our Internet website.

Copies of the Code of Business Conduct and Ethics, which appears on our website, are also available upon request by any stockholder addressed to our Corporate Secretary, 102 Witmer Road, Horsham, PA 19044.

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**ITEM 11. EXECUTIVE COMPENSATION.**

**Summary Compensation Table**

The following table provides information about all compensation earned in 2003, 2002, and 2001, by the individual who served as Chief Executive Officer during 2003, and the four other most highly compensated executive officers during 2003.

| | | Annual Compensation | | Long-term Compensation | |
|---|---|---|---|---|---|
| **Name and Principal Position** | **Year** | **Salary** | **Bonus** | **Shares Underlying Options (#)** | **All Other Compensation** |
| C. Boyd Clarke (1) | 2003 | $ 450,000 | $ 315,000 | | $ 7,300(2) |
| | 2002 | 339,231 | 254,423 | 750,000 | 397,346(3) |
| Chairman, President and Chief Executive Officer | | | | | |
| Joseph J. Villafranca (4) | 2003 | 280,000 | 140,000 | | 7,300(5) |
| | 2002 | 70,000 | 74,500 | 190,000 | 56(5) |
| Executive Vice President, Development Operations | | | | | |
| David A. Zopf | 2003 | 246,167 | 113,477 | 35,000 | 6,734(6) |
| | 2002 | 240,413 | 96,065 | 30,000 | 5,836(6) |
| Executive Vice President and Chief Scientific Officer | 2001 | 200,136 | 45,021 | 25,000 | 5,646(6) |
| Robert I. Kriebel (7) | 2003 | 250,000 | 125,000 | | 6,830(8) |
| | 2002 | 94,712 | 73,678 | 165,000 | 112(8) |
| Senior Vice President and Chief Financial Officer | | | | | |
| Debra J. Poul (9) | 2003 | 230,625 | 118,125 | 35,000 | 6,367(10) |
| | 2002 | 213,333 | 67,500 | 85,000 | 5,180(10) |
| Senior Vice President and General Counsel | 2001 | 144,933 | 20,925 | 7,500 | 4,460(10) |

(1) Mr. Clarke joined Neose in March 2002.

(2) Includes $7,000 of matching contributions in 2003 to Mr. Clarke s account in our 401(k) Plan. Also includes $300 in 2003 in premiums paid by us for group term life insurance.

(3) Includes $397,094 during 2002 of reimbursement of relocation expenses to Mr. Clarke, and $252 in premiums paid by us for group term life insurance.

(4) Dr. Villafranca joined Neose in October 2002.
(5) Includes $7,000 matching contributions in 2003 to Dr. Villafranca s account in our 401(k) plan. Also includes $300 and $56 in 2003 and 2002, respectively, in premiums paid by us for group term life insurance.
(6) Includes $6,434, $5,500, and $5,214 of matching contributions in 2003, 2002, and 2001, respectively, to Dr. Zopf s account in our 401(k) Plan. Also includes $300, $336, and $432, in 2003, 2002, and 2001, respectively, in premiums paid by us for group term life insurance.
(7) Mr. Kriebel joined Neose in August 2002.
(8) Includes $6,530 of matching contributions in 2003 to Mr. Kriebel s account in our 401(k) plan. Also includes $300 and $112 in 2003 and 2002, respectively, in premiums paid by us for group term life insurance.
(9) Ms. Poul joined Neose in January 2000 and served on a part-time basis until May 2002.
(10) Includes $6,067, $4,844, and $4,028 of matching contributions in 2003, 2002, and 2001, respectively, to Ms. Poul s account in our 401(k) Plan. Also includes $300, $336, and $432 in 2003, 2002, and 2001, respectively in premiums paid by us for group term life insurance.

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**Employment Agreements**

In March 2002, we entered into an employment agreement with C. Boyd Clarke when he joined the Company as our President and Chief Executive Officer. Under this agreement, which includes non-competition and confidentiality covenants:

The Company agreed that Mr. Clarke would receive a minimum base salary of $450,000 per year, and an annual performance incentive bonus, with a target amount of 75% of base salary, based upon the achievement of annual goals established by the Board of Directors and Mr. Clarke, which were established soon after his arrival at the Company with respect to 2002.

The Board of Directors granted Mr. Clarke options to purchase 500,000 shares of common stock at an exercise price of $32.05 per share, the fair market value on the date of grant, as follows:

an incentive stock option to purchase 12,480 shares, which option vests totally in four years from the date of grant, with 3,120 shares vested on March 29, 2003, 260 shares vesting on the last day of each of the 24 months in 2004 and 2005, and an additional 1,040 shares vesting on the last day of each of the first three months of 2006; and

a non-qualified stock option to purchase 487,520 shares, which option vests totally in four years from the date of grant, with 121,880 shares vested on March 29, 2003, and shares vesting on a monthly basis thereafter such that an aggregate of 93,750 vested during the remainder of 2003 and an aggregate of 121,880, 121,880 and 28,130 options vest 2004, 2005, and the first three months of 2006, respectively.

The Company agreed to reimburse Mr. Clarke for job-related expenses and reasonable costs related to the relocation of his residence to Pennsylvania, including travel expenses, temporary housing costs, realtor fees not to exceed $180,000, moving costs, closing costs in connection with the purchase of a new home, and $25,000 to defray additional miscellaneous expenses. Each of these payments is subject to partial repayment by Mr. Clarke in the event he resigns from Neose other than for good reason, as defined in the agreement.

In the event that Mr. Clarke is involuntarily terminated without cause or resigns for good reason (each as defined in the agreement), provided that Mr. Clarke and Neose enter into a mutual release of claims, Mr. Clarke would receive on the date of such termination a cash payment equal to one year of base salary, target annual bonus for the year in which the termination occurs, and any unpaid bonus amounts from prior years. Additionally, all outstanding options that would have vested in the 12 months following termination would immediately vest and remain exercisable for 12 months following termination.

In the event that Mr. Clarke is involuntarily terminated without cause or resigns for good reason (each as defined in the agreement) within 18 months following certain changes of control of Neose or a sale of all or substantially all of our assets in a complete liquidation or dissolution, provided that Mr. Clarke and Neose enter into a mutual release of claims, Mr. Clarke would receive on the date of such termination a cash payment equal to two years of base salary, two times the target annual bonus for the year in which termination occurs, and any unpaid bonus amounts from prior years. Additionally, all outstanding options would immediately vest and remain exercisable for 12 months following termination.

In the event that payments to Mr. Clarke under the employment agreement would result in the imposition of a parachute excise tax under Internal Revenue Code Section 4999, Mr. Clarke would be entitled to receive an additional gross-up payment to insulate him from the effect of that tax.

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In August 2002, we entered into an employment agreement with Robert I. Kriebel when he joined the Company as our Senior Vice President and Chief Financial Officer. Under this agreement:

The Company agreed that Mr. Kriebel would receive an annual salary of $250,000, a bonus of 25% of base compensation actually received for the period from August 15, 2002 through December 31, 2002, and, for succeeding years, a bonus as approved by the Compensation Committee, with a target amount of 50% of base compensation.

The Company awarded Mr. Kriebel a sign-on bonus of $50,000, which was subject to repayment if he voluntarily terminated employment with the Company or if he were terminated for cause during the first year of employment.

The Company granted Mr. Kriebel options to purchase 165,000 shares of common stock (of which 52,356 shares may be purchased through the exercise of an incentive stock option and 112,644 shares may be purchased through the exercise of a non-qualified stock option) at an exercise price of $7.64 per share, the fair market value on the date of grant.

The Company agreed to certain severance arrangements with Mr. Kriebel, which have been superseded by his change of control agreement described below.

In September 2002, we entered into an employment agreement with Joseph J. Villafranca when he joined the Company as our Senior Vice President, Pharmaceutical Development and Operations. Under this agreement, which includes non-competition and confidentiality covenants:

The Company agreed that Dr. Villafranca would receive an initial annual salary of $280,000, a bonus of $24,500 for the remainder of 2002, and, for succeeding years, a bonus with a target amount of 50% of base salary.

The Company paid Dr. Villafranca $50,000 in recognition of his foregoing certain payments from his prior employer.

The Company awarded Dr. Villafranca options to purchase 190,000 shares of common stock at an exercise price of $7.50 per share, the fair market value on the date of grant, as follows:

an incentive stock option to purchase 53,332 shares, which option became vested and exercisable with respect to 25% of the shares on each of October 1, 2002 and October 1, 2003 and will become vested and exercisable with respect to 25% of the shares on each of October 1, 2004 and October 1, 2005;

a non-qualified stock option to purchase 106,668 shares, which option became vested and exercisable with respect to 25% of the shares on each of October 1, 2002 and October 1, 2003 and will become vested and exercisable with respect to 25% of the shares on each of October 1, 2004 and October 1, 2005; and

a non-qualified stock option to purchase 30,000 shares, which option will become vested and first exercisable on the earlier of (i) the first filing with the FDA of an IND for the Company s own proprietary drug candidate that allows the Company to commence clinical trials and (ii) October 1, 2007.

In the event that Dr. Villafranca is involuntarily terminated without cause (as defined in the agreement) or due to death or disability, Dr. Villafranca would receive a cash payment equal to six months of base salary. In addition, the Company would arrange for

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outplacement services for Dr. Villafranca and provide medical benefits to him (and his spouse and dependents, if they were covered immediately prior to such termination) for six months, at a monthly cost to him equal to the monthly cost of such coverage, if any, immediately prior to such termination. If the Company s obligations result from Dr. Villafranca s termination as a result of death or disability, the cash payment under the agreement would be offset by the amount of any payments paid under life insurance or disability benefits funded by the Company.

In the event that Dr. Villafranca is involuntarily terminated without cause or resigns for good reason (each as defined in the agreement) within 12 months following certain changes of control of Neose or a sale of all or substantially all of our assets in a complete liquidation or dissolution, Dr. Villafranca would receive a cash payment equal to one year of base salary and his annual bonus for the calendar year in which the termination occurs. The Company would also arrange for outplacement services for Dr. Villafranca and provide medical benefits to him (and his spouse and dependents, if they were covered immediately prior to such termination) for 12 months, at a cost to him equal to the monthly cost of such coverage, if any immediately prior to such termination. Additionally, all outstanding options then held by Dr. Villafranca would immediately vest and remain exercisable for 12 months following termination.

In the event that payments to Dr. Villafranca under the employment agreement would result in the imposition of a parachute excise tax under Internal Revenue Code Section 4999, Dr. Villafranca would be entitled to receive an additional gross-up payment to insulate him from the effect of that tax.

**Change of Control Agreements**

During the third quarter of 2002, we entered into change of control agreements with Dr. Zopf, Mr. Kriebel, and Ms. Poul. In the event any of these executive officers is involuntarily terminated without cause (as defined in the agreement), the executive would receive on the date of termination a cash payment equal to six months base salary. We also would arrange for outplacement services for the employee and provide medical benefits to the employee (and his or her spouse and dependents, if they were covered immediately prior to such termination) for six months, at a monthly cost to the employee equal to the monthly cost of such coverage, if any, to the employee immediately prior to such termination.

In the event that any of these executive officers is involuntarily terminated without cause or resigns for good reason within 12 months following a change of control (each as defined in the agreement), the executive would receive on the date of termination a cash payment equal to one year of base salary and the employee s target annual bonus for the year in which the termination occurs. Additionally, all outstanding options that would have vested in the 12 months following termination would immediately vest and remain exercisable for 12 months following termination. We also would arrange for outplacement services for the employee and provide medical benefits to the employee (and his or her spouse and dependents, if they were covered immediately prior to such termination) for 12 months, at a monthly cost to the employee equal to the monthly cost of such coverage, if any, to the employee immediately prior to such termination. In the event payments to any executive under the change of control agreement would result in the imposition of a parachute excise tax under Section 280(G) of the Internal Revenue Code, the executive would be entitled to receive an additional gross-up payment to insulate the executive from the effect of that tax.

The change of control agreements require these executives to release us from certain claims and to comply with certain restrictive covenants. We have similar change of control agreements with our Vice Presidents.

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**Separation and Consulting Agreement**

In March 2002, we entered into a Separation and Consulting Agreement with Stephen A. Roth, Ph.D., our former Chief Executive Officer, who continues to serve on our Board of Directors. Under this agreement, Dr. Roth provided consulting services to the Chief Executive Officer and the Board of Directors for a period of 12 months, and we paid him $39,622 per month for 12 months. Dr. Roth also released us from any obligations we may have incurred in connection with his employment with us. In March 2003, Dr. Roth extended his non-competition and non-solicitation commitments for two additional years, and we will, therefore, pay him $39,622 per month for 24 additional months and his stock options will continue to vest and remain exercisable during this period. During the quarter ended March 31, 2003, we recorded a liability of $882,000, which represented the present value of the future payments, and a corresponding asset for the value of the non-competition commitment. The asset will be amortized to marketing, general and administrative expense in our statements of operations over the two-year term of the agreement.

**Compensation of Directors**

Directors who are also Neose employees receive no additional compensation for serving as a director or as a member of any Committee of the Board.

Under our standard arrangements, each non-employee director receives annually a retainer of $14,000, which may be applied, in whole or in part, toward the acquisition of an option to purchase shares of our common stock. Upon initial election or appointment to the Board of Directors, each non-employee director receives an option to purchase 30,000 shares of our common stock, and upon re-election to the Board, each non-employee director receives an option to purchase 10,000 shares of our common stock. Each automatic option grant has an exercise price equal to the fair market value on the date of grant. Each automatic grant is immediately exercisable, and has a term of ten years, subject to earlier termination, following the director s cessation of service on the Board of Directors. Any shares purchased upon exercise of the option are subject to repurchase should the director s service as a non-employee director cease prior to vesting of the shares. The initial automatic option grant of 30,000 shares vests in successive equal, annual installments over the director s initial four-year period of Board service. Each annual automatic option grant vests upon the director s completion of one year of service on the Board of Directors, as measured from the grant date. Each outstanding option vests immediately, however, upon certain changes in the ownership or control of Neose.

Non-employee directors, other than Dr. Roth, are also paid an annual retainer for service on Board Committees and are compensated for their services at each meeting of the Board or a Board Committee which they attend, at the following rates:

| Committee/Position | Retainer | Meeting Fee |
|---|---|---|
| Audit Committee | | |
| Chair | $ 8,000 | $ 3,000 |
| Member | $ 4,000 | $ 1,500 |
| Corporate Governance, Compensation and Scientific Review Committees | | |
| Chair | $ 4,000 | $ 2,000 |
| Member | $ 2,000 | $ 1,000 |

All Board members are reimbursed for their reasonable travel expenses incurred to attend meetings of the Board or Committees of the Board on which they serve.

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**Option Grant Table**

The following table provides information about grants of stock options made during 2003 to each of the executive officers named in our Summary Compensation Table.

| | Individual Grants | | | | Potential Realizable Value at Assumed Annual Rates of Stock Price Appreciation for Option Term (3) | |
|---|---|---|---|---|---|---|
| Name | Number of Shares Underlying Options Granted (1) | Percentage of Total Options Granted to Employees (2) | Exercise Price | Expiration Date | 5% | 10% |
| C. Boyd Clarke | | % | $ | | $ | $ |
| Joseph J. Villafranca | | | | | | |
| David A. Zopf | 35,000 | 6.1 | 7.45 | 02/12/14 | 163,984 | 415,568 |
| Robert I. Kriebel | | | | | | |
| Debra J. Poul | 35,000 | 6.1 | 7.45 | 02/12/14 | 163,984 | 415,568 |

(1) Each option has a term of ten years from the date of grant and vests ratably over a four-year period, beginning on the first anniversary of the date of grant.
(2) Based on the total options granted during 2003 to employees to purchase common stock.
(3) The potential realizable value of each grant is calculated assuming that the market price per share of common stock appreciates at annualized rates of 5% and 10% over the ten-year option term. The results of these calculations are based on rates set forth by the Securities and Exchange Commission and are not intended to forecast possible future appreciation of the price of our common stock.

**Aggregated Fiscal Year-End Option Values**

The following table provides information about the exercise of stock options during 2003 and the value of stock options unexercised at the end of 2003 for the executive officers named in our Summary Compensation Table. The value of unexercised stock options is calculated by multiplying the number of option shares by the differences between the option exercise price and the year-end stock price.

| | | | Number of Shares Underlying Unexercised Options | | Values of Unexercised In-The-Money Options | |
|---|---|---|---|---|---|---|
| Name | Number of Shares Acquired On Exercise | Value Realized | Exercisable | Unexercisable | Exercisable | Unexercisable |

| | | | | |
|---|---|---|---|---|
| C. Boyd Clarke | $ 281,250 | 468,750 | $ 28,125 | $ 84,375 |
| Joseph J. Villafranca | 80,000 | 110,000 | 136,000 | 187,000 |
| David A. Zopf | 102,916 | 76,250 | 1,333 | 61,250 |
| Robert I. Kriebel | 41,250 | 123,750 | 64,350 | 193,050 |
| Debra J. Poul | 32,500 | 105,000 | | 61,250 |

**Compensation Committee Interlocks and Insider Participation**

The Compensation Committee consists of Douglas J. MacMaster, Jr. (chairman), L. Patrick Gage, Ph.D., and Elizabeth H.S. Wyatt, each of whom is a non-employee director. There are no compensation committee interlocks between our Company and any other entity involving our Company s or such other entity s executive officers or board members.

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**ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT.**

The information required by this item is incorporated herein by reference to our definitive proxy statement to be filed in connection with solicitation of proxies for our Annual Meeting of Stockholders to be held on May 6, 2004.

**ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS.**

In May 2001, we entered into a tuition reimbursement agreement with A. Brian Davis, who serves as our Vice President, Finance. Under the agreement, we agreed to lend Mr. Davis the amounts necessary to pay for tuition payments and related costs and fees for an MBA degree. Interest accrues on the loan at 4.71% per year, and is payable annually beginning in May 2002. We have agreed to forgive repayment of the principal amount outstanding in four equal, annual installments commencing in May 2004 if he remains employed by us on each forgiveness date. We will forgive the accrued interest on its annual due date and, if Mr. Davis is terminated without cause, we will forgive all outstanding principal and interest. As of December 31, 2003, the amount outstanding under the agreement, including accrued interest, was $118,000.

**ITEM 14. PRINCIPAL ACCOUNTING FEES AND SERVICES.**

**Audit Fees**. The aggregate fees billed by KPMG LLP for each of the last two fiscal years for professional services rendered for the audit of the Company s annual financial statements and for the review of our interim financial statements, which are included in our Quarterly Reports on Form 10-Q, and services that are normally provided by KPMG LLP in connection with statutory and regulatory filings or engagements, are: $71,000 for 2003 and $67,000 for 2002.

**Audit-Related Fees**. The aggregate fees billed during 2003 for assurance and related services by KPMG LLP that are reasonably related to the performance of the audit or review of the Company s financial statements and are not reported under Audit Fees above are approximately $53,000. These included fees relating to preparation of a comfort letter for our resale registration statement of Form S-3, as well as consents to use of KPMG s audit opinion in other registration statement filings and fees associated with interpretation of accounting matters. We were not billed for any such services in 2002.

**Tax Fees**. The aggregate fees billed in each of the last two fiscal years for professional services rendered by KPMG LLP for tax compliance, tax advice, and tax planning are: $29,350 for 2003 and $17,000 for 2002.

**All Other Fees**. There were no fees billed in 2003 and 2002 for products and services provided by KPMG LLP, other than services reported under Audit Fees, Audit-Related Fees or Tax Fees above

**Pre-approval Policies and Procedures**. Our Audit Committee is required to pre-approve the engagement of accountants to render audit services for the Company, and any changes to the terms of the engagement are required to be pre-approved by the Audit Committee or its Chairman. Our pre-approval policies and procedures with respect to audit- and tax-related services were amended on November 4, 2003. Prior to that date, the Audit Committee was required to pre-approve all audit- and tax-related services proposed to be provided by the Company s

independent auditors, other than services for which the fees would not exceed $5,000 in any instance or 50% of the approved annual audit fees in the aggregate. The Audit Committee is now required, annually, to pre-approve the terms of the audit engagement and a description of, and budget for, the non-audit services management proposes to be provided by the Company s independent auditors during the fiscal year. Any changes or additions to the approved list or budget for non-audit services must be pre-approved by the Audit Committee or its Chairman. The required pre-approval policies and procedures were complied with during 2003, with one exception. During first quarter of 2003, the Audit Committee Chairman pre-approved the provision by KPMG LLP of tax-related services relating to compensation matters for an estimated fee of $2,000, and the final bill for such services, in the amount of $13,000, was approved by the Audit Committee after the services were rendered.

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**PART IV**

**ITEM 15. EXHIBITS, FINANCIAL STATEMENT SCHEDULES, AND REPORTS ON FORM 8-K.**

**(a) 1. Financial Statements.**

The Financial Statements filed as part of this Annual Report on Form 10-K are listed on the Index to Financial Statements on page F-1.

**2. Financial Statement Schedules.**

All financial statement schedules have been omitted here because they are not applicable, not required, or the information is shown in the Financial Statements or Notes thereto.

**3. Exhibits. (See (c) below)**

**(b) Reports on Form 8-K.**

On October 21, 2003, the Company filed a report on Form 8-K, announcing under Item 5 that it is developing an improved, GlycoPEGylated version of granulocyte colony stimulating factor (G-CSF) as its second proprietary protein.

On November 5, 2003, the Company filed a report on Form 8-K, announcing under Item 7 its financial results for the quarter ended September 30, 2003.

On November 17, 2003, the Company filed a report on Form 8-K, announcing under Item 5 that it entered into license agreements for improved therapeutic proteins with Novo Nordisk A/S.

**(c) Exhibits.**

The following is a list of exhibits filed as part of this Annual Report on Form 10-K. We are incorporating by reference to our previous SEC filings each exhibit that contains a footnote. For exhibits incorporated by reference, the location of the exhibit in the previous filing is indicated in parentheses.

| Exhibit | Description |
|---|---|

| Number | |
|---|---|
| 3.1 | Second Amended and Restated Certificate of Incorporation. (Exhibit 3.1)(1) |
| 3.2 | Second Amended and Restated By-Laws. (Exhibit 3.2)(11) |
| 3.3 | Certificate of Designation establishing and designating the Series A Junior Participating Preferred Stock. (Exhibit 3.2)(3) |
| 4.1 | See Exhibits 3.1, 3.2, and 3.3 for instruments defining rights of holders of common stock. |
| 4.2 | Representation pursuant to Item 601(b)(4)(iii)(A) of Regulation S-K. (Exhibit 4.1)(2) |
| 4.3 | Trust Indenture, dated as of March 1, 1997, between Montgomery County Industrial Development Authority and Dauphin Deposit Bank and Trust Company. (Exhibit 4.2)(2) |
| 4.4 | Form of Montgomery County Industrial Development Authority Federally Taxable Variable Rate Demand Revenue Bond (Neose Technologies, Inc. Project) Series B of 1997. (Exhibit 4.3)(2) |
| 4.5 | Amended and Restated Rights Agreement, dated as of December 3, 1998, between American Stock Transfer & Trust Company, as Rights Agent, and Neose Technologies, Inc. (Exhibit 4.1)(4) |
| 4.6 | Amendment No. 1, dated November 14, 2000, to the Amended and Restated Rights Agreement, dated as of December 3, 1998, between Neose Technologies, Inc. and American Stock Transfer & Trust Company, as Rights Agent. (Exhibit 4.1)(7) |
| 4.7 | Amendment No. 2, dated June 13, 2002, to the Amended and Restated Rights Agreement, dated as of December 3, 1998, between Neose Technologies, Inc. and American Stock Transfer & Trust Company, as Rights Agent. (Exhibit 4.1)(10) |

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| 4.8 | Amendment No. 3, dated October 30, 2002, to the Amended and Restated Rights Agreement, dated as of December 3, 1998, between Neose Technologies, Inc. and American Stock Transfer & Trust Company, as Rights Agent. (Exhibit 4.1)(12) |
| 10.1 | Amended and Restated License Agreement, dated as of February 27, 2003, between University of Pennsylvania and Neose Technologies, Inc. (Exhibit 10.1)(13) |
| 10.2 | 1995 Amended and Restated Stock Option/Stock Issuance Plan, as amended. (Appendix B)(15) |
| 10.3 | Amended and Restated Employee Stock Purchase Plan. (Appendix C)(15) |
| 10.4 | Employment Agreement, dated March 29, 2002, between C. Boyd Clarke and Neose Technologies, Inc. (Exhibit 10.1)(9) |
| 10.5 | Non-Qualified Stock Option Agreement, dated March 29, 2002, between C. Boyd Clarke and Neose Technologies, Inc. (Exhibit 10.2)(9) |
| 10.6 | Separation and Consulting Agreement, dated March 29, 2002, between Stephen A. Roth and Neose Technologies, Inc. (Exhibit 10.3)(9) |
| 10.7 | Confidentiality, intellectual Property and Non-Competition Agreement, dated March 29, 2003, between Neose Technologies, Inc. and Stephen A. Roth. (Exhibit 10.4)(14) |
| 10.8 | Employment Letter Agreement, dated August 15, 2002, between Robert I. Kriebel and Neose Technologies, Inc. (Exhibit 10.3)(11) |
| 10.9 | Change of Control Agreement, dated October 7, 2002, between Robert I. Kriebel and Neose Technologies, Inc. (Exhibit 10.4)(11) |
| 10.10 | Employment Agreement, dated September 12, 2002, between Joseph J. Villafranca and Neose Technologies, Inc. (Exhibit 10.5)(11) |
| 10.11 | Form of Change of Control Agreement between Neose Technologies, Inc. and Certain Officers. (Exhibit 10.1)(11) |
| 10.12 | Change of Control Agreement, dated October 7, 2002, between Debra J. Poul and Neose Technologies, Inc. (Exhibit 10.2)(11) |
| 10.13 | Loan Agreement, dated as of March 1, 1997, between Montgomery County Industrial Development Authority and Neose Technologies, Inc. (Exhibit 10.1)(2) |
| 10.14 | Participation and Reimbursement Agreement, dated as of March 1, 1997, between Jefferson Bank and CoreStates Bank, N.A. (Exhibit 10.2)(2) |
| 10.15 | Form of CoreStates Bank, N.A. Irrevocable Letter of Credit. (Exhibit 10.3)(2) |
| 10.16 | Pledge, Security and Indemnification Agreement, dated as of March 1, 1997, by and among CoreStates Bank, N.A., Jefferson Bank, and Neose Technologies, Inc. (Exhibit 10.4)(2) |
| 10.1 | Reimbursement Agreement, dated as of March 1, 1997, between Jefferson Bank and Neose Technologies, Inc. (Exhibit 10.5)(2) |
| 10.18 | Specimen of Note from Company to Jefferson Bank. (Exhibit 10.6)(2) |
| 10.19 | Mortgage, Assignment and Security Agreement, dated March 20, 1997, between Jefferson Bank and Neose Technologies, Inc. (Exhibit 10.7)(2) |
| 10.20 | Security Agreement, dated as of March 1, 1997, by and between Jefferson Bank and Neose Technologies, Inc. (Exhibit 10.8)(2) |
| 10.21 | Assignment of Contract, dated as of March 20, 1997, between Jefferson Bank and Neose Technologies, Inc. (Exhibit 10.9)(2) |
| 10.22 | Custodial and Collateral Security Agreement, dated as of March 20, 1997, by and among Offitbank, Jefferson Bank, and Neose Technologies, Inc. (Exhibit 10.10)(2) |
| 10.23 | Placement Agreement, dated March 20, 1997, among Montgomery County Industrial Development Authority, CoreStates Capital Markets, and Neose Technologies, Inc. (Exhibit 10.11)(2) |
| 10.24 | Remarketing Agreement, dated as of March 1, 1997, between CoreStates Capital Markets and Neose Technologies, Inc. (Exhibit 10.12)(2) |

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| 10.25 | Operating Agreement of Magnolia Nutritionals LLC, dated October 12, 1999, between Neose Technologies, Inc. and McNeil PPC, Inc. acting through its division McNeil Specialty Products Company. (Exhibit 99.2)(5) |
| 10.26 | Collaboration and License Agreement, dated November 3, 1999, between Neose Technologies, Inc. and American Home Products Corporation. (Exhibit 99.3)(5) |
| 10.27 | Modification Agreement Relating To Reimbursement Agreements, dated as of May 1, 2000, between Hudson United Bank, Jefferson Bank Division, successor to Jefferson Bank, and Neose Technologies, Inc. (Exhibit 10.1)(6) |
| 10.28 | Modification Agreement Relating to Custodial Bank Agreement, dated as of May 1, 2000, by and among Offitbank, Hudson United Bank, Jefferson Bank Division, successor to Jefferson Bank, and Neose Technologies, Inc. (Exhibit 10.2)(6) |
| 10.29 | Agreement of Lease, dated as of February 15, 2002, between Liberty Property Leased Partnership and Neose Technologies, Inc. (Exhibit 10.40)(8) |
| 10.30 | Standard Industrial/Commercial Multi-Tenant Lease-Net, dated February 2, 2001, between Nancy Ridge Technology Center, LLC and Neose Technologies, Inc. (Exhibit 10.47)(8) |
| 10.31 | First Amendment to Lease, dated May 18, 2001, between Nancy Ridge Technology Center, LLC and Neose Technologies, Inc. (Exhibit 10.48)(8) |
| 10.32 | Agreement, dated as of August 24, 2001, between IPS and Neose Technologies, Inc. (Exhibit 10.49)(8) |
| 10.33 | Master Security Agreement between General Electric Capital Corporation and Neose Technologies, Inc., dated as of December 19, 2002. (Exhibit 10.33)(13) |
| 10.34 | Amendment to Master Security Agreement between General Electric Capital Corporation and Neose Technologies, Inc., dated as of December 19, 2002. (Exhibit 10.34)(13) |
| 10.35 | Promissory Note of Neose Technologies, Inc. to General Electric Capital Corporation, dated December 27, 2002. (Exhibit 10.35)(13) |
| 10.36 | Promissory Note of Neose Technologies, Inc. to General Electric Capital Corporation, dated March 28, 2003. (Exhibit 10.3)(14) |
| 10.37 | Promissory Note of Neose Technologies, Inc. to General Electric Capital Corporation, dated September 17, 2003. (Exhibit 10.1)(16) |
| 10.38 | Common Stock Purchase Agreement between Neose Technologies, Inc. and the Purchasers, dated as of February 13, 2003. (Exhibit 10.39)(13) |
| 10.39*# | Research, Development and License Agreement between Neose Technologies, Inc. and Novo Nordisk A/S dated as of November 17, 2003. |
| 10.40*# | Research, Development and License Agreement among Neose Technologies, Inc. and Novo Nordisk A/S and Novo Nordisk Health Care AG dated as of November 17, 2003. |
| 10.41*# | Amendment to Research, Development and License Agreement between Neose Technologies, Inc. and Novo Nordisk A/S dated December 18, 2003. |
| 10.42*# | Amendment to Research, Development and License Agreement among Neose Technologies, Inc. and Novo Nordisk A/S and Novo Nordisk Health Care AG dated December 18, 2003. |
| 10.43* | Promissory Note of NeoseTechnologies, Inc. to General Electric Capital Corporation, dated December 18, 2003. |
| 10.44* | Credit Agreement by and between Brown Brothers Harriman & Co. and Neose Technologies, Inc., dated as of January 30, 2004. |
| 10.45* | General Security Agreement by Neose Technologies, Inc. to Brown Brothers Harriman & Co., dated as of January 30, 2004. |
| 10.46* | Open-end Mortgage and Security Agreement by and between Neose Technologies, Inc. and Brown Brothers Harriman & Co., dated as of January 30, 2004. |
| 10.47* | Term Loan Note of Neose Technologies, Inc. to Brown Brothers Harriman & Co., dated January 30, 2004. |
| 23.1* | Consent of KPMG LLP. |

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|---|---|
| 23.2* | Information Regarding Consent of Arthur Andersen LLP. |
| 24* | Powers of Attorney (included as part of signature page hereof). |
| 31.1* | Certification by Chief Executive Officer pursuant to Rule 13a-14(a) and 15d-14(a), as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002. |
| 31.2* | Certification by Chief Financial Officer pursuant to Rule 13-14(a) and 15d-14(a), as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002. |
| 32.1* | Certification Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002. |
| 32.2* | Certification Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002. |

* Filed herewith.

Portions of this Exhibit were omitted and filed separately with the Secretary of the SEC pursuant to an order of the SEC granting our application for confidential treatment filed pursuant to Rule 406 under the Securities Act.

Compensation plans and arrangements for executives and others.

\# Portions of this Exhibit were omitted and filed separately with the Secretary of the SEC pursuant to a request for confidential treatment that has been filed with the SEC.

(1) Filed as an Exhibit to our Registration Statement on Form S-1 (Registration No. 33-80693) filed with the SEC on December 21, 1995, as amended.
(2) Filed as an Exhibit to our Quarterly Report on Form 10-Q for the quarterly period ended March 31, 1997.
(3) Filed as an Exhibit to our Current Report on Form 8-K filed with the SEC on October 1, 1997.
(4) Filed as an Exhibit to our Current Report on Form 8-K filed with the SEC on January 8, 1999.
(5) Filed as an Exhibit to our Current Report on Form 8-K filed with the SEC on February 2, 2000.
(6) Filed as an Exhibit to our Quarterly Report on Form 10-Q for the quarterly period ended June 30, 2000.
(7) Filed as an Exhibit to our Current Report on Form 8-K filed with the SEC on November 15, 2000.
(8) Filed as an Exhibit to our Annual Report on Form 10-K filed with the SEC on March 29, 2002.
(9) Filed as an Exhibit to our Current Report on Form 8-K/A filed with the SEC on April 30, 2002.
(10) Filed as an Exhibit to our Current Report on Form 8-K filed with the SEC on June 13, 2002.
(11) Filed as an Exhibit to our Quarterly Report on Form 10-Q for the quarterly period ended September 30, 2002.
(12) Filed as an Exhibit to our Current Report on Form 8-K filed with the SEC on October 31, 2002.
(13) Filed as an Exhibit to our Annual Report on Form 10-K for the year ended December 31, 2002.
(14) Filed as an Exhibit to our Quarterly Report on Form 10-Q for the quarterly period ended March 31, 2003.
(15) Filed as an Exhibit to our Proxy Statement filed with the SEC on April 1, 2003.
(16) Filed as an Exhibit to our Quarterly Report on Form 10-Q for the quarterly period ended September 30, 2003.

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SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, we have duly caused this report to be signed on our behalf by the undersigned, thereunto duly authorized.

NEOSE TECHNOLOGIES, INC.

Date: February 17, 2004

By: /s/ C. Boyd Clarke

Chairman, President and Chief Executive Officer

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of Neose and in the capacities and on the dates indicated.

Each person, in so signing also makes, constitutes, and appoints C. Boyd Clarke, Robert I. Kriebel and A. Brian Davis, and each of them acting alone, as his or her true and lawful attorneys-in-fact, with full power of substitution, in his name, place, and stead, to execute and cause to be filed with the Securities and Exchange Commission any or all amendments to this report.

| Name | Capacity | Date |
|---|---|---|
| /s/ C. Boyd Clarke | Chairman, President and Chief Executive Officer (Principal Executive Officer) | February 17, 2004 |
| /s/ Robert I. Kriebel<br>Robert I. Kriebel | Senior Vice President and Chief Financial Officer (Principal Financial Officer) | February 17, 2004 |
| /s/ Brian H. Dovey<br>Brian H. Dovey | Director | February 17, 2004 |
| /s/ L. Patrick Gage<br>L. Patrick Gage | Director | February 17, 2004 |
| /s/ William F. Hamilton<br>William F. Hamilton | Director | February 17, 2004 |
| /s/ Douglas J. MacMaster, Jr.<br>Douglas J. MacMaster, Jr. | Director | February 17, 2004 |

| | | |
|---|---|---|
| /s/ Mark H. Rachesky | Director | February 17, 2004 |
| Mark H. Rachesky | | |
| /s/ Stephen A. Roth | Director | February 17, 2004 |
| Stephen A. Roth | | |
| /s/ Lowell E. Sears | Director | February 17, 2004 |
| Lowell E. Sears | | |
| /s/ Elizabeth H.S. Wyatt | Director | February 17, 2004 |
| Elizabeth H.S. Wyatt | | |

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**INDEPENDENT AUDITORS REPORT**

The Board of Directors and Stockholders

Neose Technologies, Inc.:

We have audited the accompanying balance sheets of Neose Technologies, Inc. (a development-stage company) as of December 31, 2003 and 2002, and the related statements of operations, stockholders equity and comprehensive loss, and cash flows for each of the years in the two-year period ended December 31, 2003, and for the period from January 17, 1989 (inception) to December 31, 2003. These financial statements are the responsibility of the Company s management. Our responsibility is to express an opinion on these financial statements based on our audits. The financial statements of Neose Technologies, Inc. for the year ended December 31, 2001 and for the period from January 17, 1989 (inception) to December 31, 2003, to the extent related to the period from January 17, 1989 (inception) to December 31, 2001, were audited by other auditors who have ceased operations. Those auditors expressed an unqualified opinion on those financial statements in their report dated January 25, 2002. Our opinion on the statements of operations, stockholders equity and comprehensive loss, and cash flows, insofar as it relates to the amounts included for the period from January 17, 1989 (inception) to December 31, 2001, is based solely on the report of the other auditors.

We conducted our audits in accordance with auditing standards generally accepted in the United States of America. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, based on our audits and the report of other auditors, the financial statements referred to above present fairly, in all material respects, the financial position of Neose Technologies, Inc. (a development-stage company) as of December 31, 2003 and 2002, and the results of its operations and its cash flows for each of the years in the two-year period ended December 31, 2003, and for the period from January 17, 1989 (inception) to December 31, 2003, in conformity with accounting principles generally accepted in the United States of America.

/s/ KPMG LLP

Philadelphia, Pennsylvania

February 3, 2004

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The following is a copy of a report issued by Arthur Andersen LLP and included in the 2001 Form 10-K/A report for the fiscal year ended December 31, 2001 filed on April 30, 2002. This report has not been reissued by Arthur Andersen LLP, and Arthur Andersen LLP has not consented to its use in this Annual Report on Form 10-K. For further discussion, see Exhibit 23.2 to this Form 10-K.

Report of Independent Public Accountants

To Neose Technologies, Inc.:

We have audited the accompanying consolidated balance sheets of Neose Technologies, Inc. (a Delaware corporation in the development stage) and subsidiaries as of December 31, 2000 and 2001, and the related consolidated statements of operations, stockholders equity and comprehensive loss, and cash flows for each of the three years in the period ended December 31, 2001, and for the period from inception (January 17, 1989) to December 31, 2001. These financial statements are the responsibility of the Company s management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with auditing standards generally accepted in the United States. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of Neose Technologies, Inc. and subsidiaries as of December 31, 2000 and 2001, and the results of their operations and their cash flows for each of the three years in the period ended December 31, 2001, and for the period from inception (January 17, 1989) to December 31, 2001, in conformity with accounting principles generally accepted in the United States.

ARTHUR ANDERSEN LLP

Philadelphia, Pennsylvania

January 25, 2002

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**Neose Technologies, Inc.**

(a development-stage company)

**Balance Sheets**

(in thousands, except per share amounts)

| | December 31, 2002 | December 31, 2003 |
|---|---|---|
| **Assets** | | |
| Current assets: | | |
| Cash and cash equivalents | $ 31,088 | $ 48,101 |
| Marketable securities | 9,952 | 4,959 |
| Restricted funds | 977 | 901 |
| Prepaid expenses and other current assets | 558 | 917 |
| Total current assets | 42,575 | 54,878 |
| Property and equipment, net | 36,508 | 37,192 |
| Acquired intellectual property, net | 2,507 | 1,910 |
| Other assets | 1,502 | 865 |
| Total assets | $ 83,092 | $ 94,845 |
| **Liabilities and Stockholders Equity** | | |
| Current liabilities: | | |
| Current portion of long-term debt and capital lease obligations | $ 1,851 | $ 2,231 |
| Accounts payable | 1,127 | 2,342 |
| Accrued compensation | 1,339 | 2,510 |
| Accrued expenses | 1,880 | 2,433 |
| Deferred revenue | 320 | 4,333 |
| Total current liabilities | 6,517 | 13,849 |
| Long-term debt and capital lease obligations | 5,560 | 8,370 |
| Other liabilities | 330 | 413 |
| Total liabilities | 12,407 | 22,632 |
| Commitments (Note 14) | | |
| Stockholders equity: | | |
| Preferred stock, $.01 par value, 5,000 shares authorized, none issued | | |
| Common stock, $.01 par value, 30,000 shares authorized; 14,330 and 19,935 shares issued; 14,324 and 19,935 shares outstanding | 143 | 199 |
| Additional paid-in capital | 178,945 | 217,849 |
| Treasury stock, 6 shares at cost | (175) | |
| Deferred compensation | (170) | (96) |
| Deficit accumulated during the development-stage | (108,058) | (145,739) |

| | | |
|---|---|---|
| Total stockholders equity | 70,685 | 72,213 |
| Total liabilities and stockholders equity | $ 83,092 | $ 94,845 |

The accompanying notes are an integral part of these financial statements.

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**Neose Technologies, Inc.**

(a development-stage company)

**Statements of Operations**

(in thousands, except per share amounts)

| | Year Ended December 31, | | | Period from inception (January 17, 1989) to December 31, 2003 |
|---|---|---|---|---|
| | 2001 | 2002 | 2003 | |
| Revenue from collaborative agreements | $ 1,266 | $ 4,813 | $ 1,435 | $ 18,881 |
| Operating expenses: | | | | |
| Research and development | 14,857 | 21,481 | 26,821 | 126,499 |
| Marketing, general and administrative | 9,374 | 12,510 | 11,148 | 60,220 |
| Total operating expenses | 24,231 | 33,991 | 37,969 | 186,719 |
| Operating loss | (22,965) | (29,178) | (36,534) | (167,838) |
| Other income | 6,120 | 1,653 | | 7,773 |
| Impairment of equity securities | | | (1,250) | (1,250) |
| Interest income | 3,704 | 1,108 | 564 | 19,342 |
| Interest expense | (188) | | (461) | (3,766) |
| Net loss | $ (13,329) | $ (26,417) | $ (37,681) | $ (145,739) |
| Basic and diluted net loss per share | $ (0.95) | $ (1.85) | $ (2.14) | |
| Weighted-average shares outstanding used in computing basic and diluted net loss per share | 14,032 | 14,259 | 17,611 | |

The accompanying notes are an integral part of these financial statements.

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**Neose Technologies, Inc.**

(a development-stage company)

**Statements of Stockholders Equity and Comprehensive Loss**

(in thousands)

| | Convertible Preferred Stock | | Common Stock | | Additional | | | Deficit accumulated during the development stage | Unrealized gains on marketable securities | Comprehensive loss accumulated during the development stage |
|---|---|---|---|---|---|---|---|---|---|---|
| | Shares | Amount | Shares | Amount | paid-in capital | Treasury stock | Deferred compensation | | | |
| Balance, January 17, 1989 (inception) | | $ | | $ | $ | $ | $ | $ | $ | $ |
| Initial issuance of common stock | | | 1,302 | 13 | (3) | | | | | |
| Shares issued pursuant to consulting, licensing, and antidilutive agreements | | | 329 | 3 | (1) | | | | | |
| Sale of common stock | | | 133 | 1 | 1 | | | | | |
| Net loss | | | | | | | | (460) | | (460) |
| Balance, December 31, 1990 | | | 1,764 | 17 | (3) | | | (460) | | (460) |
| Sale of stock | 1,517 | 15 | 420 | 4 | 4,499 | | (7) | | | |
| Shares issued pursuant to consulting and antidilutive agreements | | | 145 | 1 | | | | | | |
| Capital contributions | | | | | 10 | | | | | |
| Dividends on preferred stock | | | | | (18) | | | | | |
| Net loss | | | | | | | | (1,865) | | (1,865) |
| Balance, December 31, 1991 | 1,517 | 15 | 2,329 | 22 | 4,488 | | (7) | (2,325) | | (2,325) |
| Sale of stock | 260 | 2 | 17 | | 2,344 | | | | | |
| Shares issued pursuant to redemption of notes payable | | | 107 | 1 | 682 | | | | | |
| Exercise of stock options and warrants | | | 21 | | 51 | | | | | |
| Amortization of deferred compensation | | | | | | | 5 | | | |
| Dividends on preferred stock | | | | | (36) | | | | | |
| Net loss | | | | | | | | (3,355) | | (3,355) |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Balance, December 31, 1992 | 1,777 | 17 | 2,474 | 23 | 7,529 | | (2) | (5,680) | | (5,680) |
| Sale of preferred stock | 250 | 3 | | | 1,997 | | | | | |
| Shares issued to licensor | | | 3 | | | | | | | |
| Shares issued to preferred stockholder in lieu of cash dividends | | | 1 | | 18 | | | | | |
| Amortization of deferred compensation | | | | | | | 2 | | | |
| Dividends on preferred stock | | | | | (36) | | | | | |
| Net loss | | | | | | | | (2,423) | | (2,423) |
| Balance, December 31, 1993 | 2,027 | 20 | 2,478 | 23 | 9,508 | | | (8,103) | | (8,103) |
| Sale of preferred stock | 2,449 | 25 | | | 11,040 | | | | | |
| Exercise of stock options | | | 35 | 1 | 14 | | | | | |
| Shares issued to preferred stockholder in lieu of cash dividends | | | 10 | 1 | 53 | | | | | |
| Dividends on preferred stock | | | | | (18) | | | | | |
| Net loss | | | | | | | | (6,212) | | (6,212) |
| Balance, December 31, 1994 | 4,476 | $ 45 | 2,523 | $ 25 | $ 20,597 | $ | $ | $ (14,315) | $ | $ (14,315) |

(continued)

The accompanying notes are an integral part of these financial statements.

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**Neose Technologies, Inc.**

(a development-stage company)

**Statements of Stockholders Equity and Comprehensive Loss**

(continued)

(in thousands)

| | Convertible Preferred Stock | | Common Stock | | Additional | | | Deficit accumulated during the development stage | Unrealized gains on marketable securities | Comprehensive loss accumulated during the development stage |
|---|---|---|---|---|---|---|---|---|---|---|
| | Shares | Amount | Shares | Amount | paid-in capital | Treasury stock | Deferred compensation | | | |
| Sale of preferred stock | 2,721 | $ 27 | | $ | $ 10,065 | $ | $ | $ | $ | $ |
| Exercise of stock options and warrants | | | 116 | 1 | 329 | | | | | |
| Shares issued to employees in lieu of cash compensation | | | 8 | | 44 | | | | | |
| Deferred compensation related to grant of stock options | | | | | 360 | | (360) | | | |
| Shares issued to stockholder related to the initial public offering | | | 23 | | | | | | | |
| Shares issued to preferred stockholder in lieu of cash dividends | | | 3 | | 18 | | | | | |
| Dividends on preferred stock | | | | | (36) | | | | | |
| Conversion of preferred stock into common stock | (1,417) | (14) | 472 | 5 | 9 | | | | | |
| Net loss | | | | | | | | (5,067) | | (5,067) |
| Balance, December 31, 1995 | 5,780 | 58 | 3,145 | 31 | 31,386 | | (360) | (19,382) | | (19,382) |
| Dividends on preferred stock | | | | | (18) | | | | | |
| Sale of common stock in initial public offering | | | 2,588 | 26 | 29,101 | | | | | |
| Conversion of preferred stock into common stock | (5,780) | (58) | 2,411 | 24 | 34 | | | | | |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Exercise of stock options and warrants | | 65 | 1 | 162 | | | | | |
| Shares issued pursuant to employee stock purchase plan | | 6 | | 60 | | | | | |
| Stock-based compensation related to modification of options | | | | 106 | | | | | |
| Amortization of deferred compensation | | | | | | 90 | | | |
| Net loss | | | | | | | (6,141) | | (6,141) |
| Balance, December 31, 1996 | | 8,215 | 82 | 60,831 | | (270) | (25,523) | | (25,523) |
| Sale of common stock in public offering | | 1,250 | 13 | 20,326 | | | | | |
| Exercise of stock options and warrants | | 42 | | 139 | | | | | |
| Shares issued pursuant to employee stock purchase plan | | 18 | | 189 | | | | | |
| Deferred compensation related to grants of stock options | | | | 322 | | (322) | | | |
| Amortization of deferred compensation | | | | | | 231 | | | |
| Net loss | | | | | | | (9,064) | | (9,064) |
| Balance, December 31, 1997 | $ | 9,525 | $ 95 | $ 81,807 | $ | $ (361) | $ (34,587) | $ | $ (34,587) |

(continued)

The accompanying notes are an integral part of these financial statements.

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**Neose Technologies, Inc.**

(a development-stage company)

**Statements of Stockholders Equity and Comprehensive Loss**

(continued)

(in thousands)

| | Convertible Preferred Stock | | Common Stock | | Additional paid-in capital | Treasury stock | Deferred compensation | Deficit accumulated during the development stage | Unrealized gains on marketable securities | Comprehensive loss accumulated during the development stage |
|---|---|---|---|---|---|---|---|---|---|---|
| | Shares | Amount | Shares | Amount | | | | | | |
| Exercise of stock options | | $ | 49 | $ 1 | $ 261 | $ | $ | $ | $ | $ |
| Shares issued pursuant to employee stock purchase plan | | | 15 | | 171 | | | | | |
| Deferred compensation related to grants of stock options | | | | | 161 | | (161) | | | |
| Amortization of deferred compensation | | | | | | | 311 | | | |
| Unrealized gains on marketable securities | | | | | | | | | 222 | 222 |
| Net loss | | | | | | | | (11,907) | | (11,907) |
| Balance, December 31, 1998 | | | 9,589 | 96 | 82,400 | | (211) | (46,494) | 222 | (46,272) |
| Sales of common stock in private placements | | | 1,786 | 18 | 17,398 | | | | | |
| Exercise of stock options and warrants | | | 43 | | 263 | | | | | |
| Shares issued pursuant to employee stock purchase plan | | | 16 | | 156 | | | | | |
| Deferred compensation related to grants of stock options | | | | | 796 | | (796) | | | |
| Amortization of deferred compensation | | | | | | | 477 | | | |
| Unrealized losses on marketable securities | | | | | | | | | (222) | (222) |
| Net loss | | | | | | | | (13,318) | | (13,318) |
| Balance, December 31, 1999 | | | 11,434 | 114 | 101,013 | | (530) | (59,812) | | (59,812) |
| Sale of common stock in public offering | | | 2,300 | 23 | 68,582 | | | | | |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Exercise of stock options and warrants | | 247 | 3 | 2,735 | | | | | |
| Shares issued pursuant to employee stock purchase plan | | 11 | | 157 | | | | | |
| Deferred compensation related to grants of employee stock options | | | | 70 | | (70) | | | |
| Deferred compensation related to non-employee stock options | | | | 1,200 | | (1,200) | | | |
| Amortization of deferred compensation related to: | | | | | | | | | |
| Employee options | | | | | | 70 | | | |
| Non-employee options | | | | | | 1,013 | | | |
| Net loss | | | | | | | (8,500) | | (8,500) |
| Balance, December 31, 2000 | $ | 13,992 | $ 140 | $ 173,757 | $ | $ (717) | $ (68,312) | $ | $ (68,312) |

(continued)

The accompanying notes are an integral part of these financial statements.

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**Neose Technologies, Inc.**

(a development-stage company)

**Statements of Stockholders Equity and Comprehensive Loss**

(continued)

(in thousands)

| | Convertible Preferred Stock | | Common Stock | | Additional | | | Deficit | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Shares | Amount | Shares | Amount | paid-in Capital | Treasury stock | Deferred compensation | accumulated during the development stage | Unrealized gains on marketable securities | Comprehensive loss accumulated during the development stage |
| Exercise of stock options and warrants | | $ | 79 | $ 1 | $ 867 | $ | $ | $ | $ | $ |
| Shares issued pursuant to employee stock purchase plan | | | 18 | | 335 | | | | | |
| Acquisition of treasury stock, 6 shares at cost | | | (6) | | | (175) | | | | |
| Deferred compensation related to grants of employee stock options | | | | | 299 | | (299) | | | |
| Deferred compensation related to non-employee stock options | | | | | 75 | | (75) | | | |
| Stock-based compensation related to modifications of options | | | | | 791 | | | | | |
| Amortization of deferred compensation related to: | | | | | | | | | | |
| Employee options | | | | | | | 125 | | | |
| Non-employee options | | | | | | | 463 | | | |
| Net loss | | | | | | | | (13,329) | | (13,329) |
| Balance, December 31, 2001 | | | 14,083 | 141 | 176,124 | (175) | (503) | (81,641) | | (81,641) |
| Exercise of stock options | | | 209 | 2 | 1,575 | | | | | |
| Shares issued pursuant to employee stock purchase plan | | | 32 | | 384 | | | | | |
| Deferred compensation related to grants of employee stock options | | | | | 118 | | (118) | | | |
| | | | | | (878) | | 878 | | | |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Deferred compensation related to non-employee stock options | | | | | | | | | |
| Stock-based compensation related to modification of options | | | | 1,622 | | | | | |
| Amortization of deferred compensation related to: | | | | | | | | | |
| Employee options | | | | | | 171 | | | |
| Non-employee options | | | | | | (598) | | | |
| Net loss | | | | | | | (26,417) | | (26,417) |
| Balance, December 31, 2002 | $ | 14,324 | $ 143 | $ 178,945 | $ (175) | $ (170) | $ (108,058) | $ | $ (108,058) |

(continued)

The accompanying notes are an integral part of these financial statements.

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**Neose Technologies, Inc.**

(a development-stage company)

**Statements of Stockholders Equity and Comprehensive Loss**

(continued)

(in thousands)

| | Convertible Preferred Stock | | Common Stock | | Additional | | | Deficit accumulated during the development stage | Unrealized gains on marketable securities | Comprehensive loss accumulated during the development stage |
|---|---|---|---|---|---|---|---|---|---|---|
| | Shares | Amount | Shares | Amount | paid-in Capital | Treasury stock | Deferred compensation | | | |
| Sale of common stock in a registered offering | | $ | 2,655 | $ 26 | $ 22,351 | $ | $ | $ | $ | $ |
| Sale of common stock in a private placement | | | 2,867 | 29 | 16,291 | | | | | |
| Exercise of stock options | | | 63 | 1 | 171 | | | | | |
| Shares issued pursuant to employee stock purchase plan | | | 26 | | 21 | 175 | | | | |
| Deferred compensation related to grants of employee stock options | | | | | 56 | | (56) | | | |
| Deferred compensation related to non-employee stock options | | | | | 14 | | (14) | | | |
| Amortization of deferred compensation related to: | | | | | | | | | | |
| Employee options | | | | | | | 100 | | | |
| Non-employee options | | | | | | | 44 | | | |
| Net loss | | | | | | | | (37,681) | | (37,681) |
| Balance, December 31, 2003 | | $ | 19,935 | $ 199 | $ 217,849 | $ | $ (96) | $ (145,739) | $ | $ (145,739) |

The accompanying notes are an integral part of these financial statements

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**Neose Technologies, Inc.**

(a development-stage company)

**Statements of Cash Flows**

(in thousands)

| | Year ended December 31, | | | Period from inception (January 17, 1989) to |
|---|---|---|---|---|
| | 2001 | 2002 | 2003 | December 31, 2003 |
| Cash flows from operating activities: | | | | |
| Net loss | $ (13,329) | $ (26,417) | $ (37,681) | $ (145,739) |
| Adjustments to reconcile net loss to cash used in operating activities: | | | | |
| Depreciation and amortization | 2,422 | 2,376 | 4,818 | 17,927 |
| Loss on disposition of property and equipment | | | 264 | 264 |
| Non-cash compensation | 1,379 | 1,195 | 144 | 4,917 |
| Common stock issued for non-cash and other charges | | | | 35 |
| Changes in operating assets and liabilities: | | | | |
| Prepaid expenses and other current and non-current assets | (1,052) | 825 | (421) | (1,231) |
| Accounts payable | 636 | 408 | 1,215 | 2,342 |
| Accrued compensation | 254 | 484 | 708 | 2,091 |
| Accrued expenses | (208) | 734 | (200) | 1,578 |
| Deferred revenue | 833 | (902) | 4,013 | 4,333 |
| Other liabilities | | 330 | (336) | (6) |
| Net cash used in operating activities | (9,065) | (20,967) | (27,476) | (113,489) |
| Cash flows from investing activities: | | | | |
| Purchases of property and equipment | (9,371) | (17,826) | (3,455) | (50,563) |
| Proceeds from sale-leaseback of equipment | | | | 1,382 |
| Purchases of marketable securities | (103,465) | (60,411) | (38,569) | (423,307) |
| Proceeds from sales of marketable securities | | | 18,219 | 29,686 |
| Proceeds from maturities of and other changes in marketable securities | 131,238 | 51,000 | 25,500 | 389,360 |
| Purchase of acquired technology | | | | (4,550) |
| Investment in equity securities | | | | (1,250) |
| Impairment of equity securities | | | 1,250 | 1,250 |
| Net cash provided by (used in) investing activities | 18,402 | (27,237) | 2,945 | (57,992) |
| Cash flows from financing activities: | | | | |
| Proceeds from issuance of debt | | 2,261 | 4,987 | 19,203 |
| Repayments of debt | (1,100) | (1,100) | (2,584) | (10,736) |
| Restricted cash related to debt | (9) | (75) | 76 | (830) |
| Proceeds from issuance of preferred stock, net | | | | 29,497 |

| | | | | |
|---|---|---|---|---|
| Proceeds from issuance of common stock, net | 335 | 384 | 38,893 | 176,117 |
| Proceeds from exercise of stock options and warrants | 868 | 1,577 | 172 | 6,578 |
| Acquisition of treasury stock | (175) | | | (175) |
| Dividends paid | | | | (72) |
| Net cash provided by (used in) financing activities | (81) | 3,047 | 41,544 | 219,582 |
| Net increase (decrease) in cash and cash equivalents | 9,256 | (45,157) | 17,013 | 48,101 |
| Cash and cash equivalents, beginning of period | 66,989 | 76,245 | 31,088 | |
| Cash and cash equivalents, end of period | $ 76,245 | $ 31,088 | $ 48,101 | $ 48,101 |

The accompanying notes are an integral part of these financial statements

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**Neose Technologies, Inc.**

(a development-stage company)

**Notes to Financial Statements**

**Note 1. Background**

We are a biopharmaceutical company focused on improving protein therapeutics using our proprietary technologies. Our core technologies, GlycoAdvance and GlycoPEGylation, enable us to manipulate, enzymatically, the carbohydrate structures of glycoproteins, and thereby pursue the objective of improving the therapeutic profiles of proteins that have already been marketed or substantially developed. Our business strategy is to use our technologies to improve proteins for which there exists a substantial body of data demonstrating safety and efficacy. We intend to apply this strategy to next-generation products that we are developing on our own or in collaboration with others. We also expect to use our technologies, through strategic partners, to improve products of other parties. Neose was initially incorporated in January 1989, and began operations in October 1990.

**Note 2. Summary of Significant Accounting Policies**

*Use of Estimates*

The preparation of financial statements in conformity with accounting principles generally accepted in the United States of America requires us to make estimates and assumptions. Those estimates and assumptions affect the reported amounts of assets and liabilities as of the date of the financial statements, the disclosure of contingent assets and liabilities as of 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.

*Cash and Cash Equivalents*

We consider all highly liquid investments with a maturity of three months or less on the date of purchase to be cash equivalents. As of December 31, 2002 and 2003, cash equivalents consisted of securities and obligations of either the U.S. Treasury or U.S. government agencies. Our cash balances have been kept on deposit primarily at one bank and in amounts greater than $100,000, which is the limit of insurance provided by the Federal Deposit Insurance Corporation.

*Marketable Securities*

Marketable securities consist of investments that have a maturity of more than three months on the date of purchase. To help maintain the safety and liquidity of our marketable securities, we have established guidelines for the concentration, maturities, and credit ratings of our investments. We determine the appropriate classification of our debt securities at the time of purchase and re-evaluate such designation as of each balance sheet date. Marketable securities that we have the positive intent and ability to hold to maturity are classified as held-to-maturity securities and recorded at amortized cost.

As of December 31, 2003, we held a marketable security that was an obligation of a U.S. government agency. The security, which is classified as held-to-maturity, had an original maturity of 11 months. As of December 31, 2003, the security s amortized cost was $4,959,000, which included $15,000 of accrued interest, and the fair value was $4,961,000. During 2003, there was $342,000 of interest earned on securities that matured during the year.

*Restricted Funds*

Under the terms of our Montgomery County (Pennsylvania) Industrial Development Authority taxable bonds, we are required to make monthly payments to an escrow account to provide for an annual prepayment of principal. As of December 31, 2003, we had restricted funds of $901,000, which consisted of our monthly payments plus interest earned on the balance of the account. During the first quarter of 2004, we expect to use the restricted funds and a portion of the proceeds under the credit agreement we entered into in January 2004 to pay in full the outstanding balance of the taxable bonds. See Note 7 for a description of the credit agreement.

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**Neose Technologies, Inc.**

(a development-stage company)

**Notes to Financial Statements**

*Property and Equipment*

Property and equipment are stated at cost. Property and equipment capitalized under capital leases are recorded at the present value of the minimum lease payments due over the lease term. Depreciation and amortization are provided using the straight-line method over the estimated useful lives of the related assets or the lease term, whichever is shorter. We use depreciable lives of three to seven years for laboratory and office equipment, and three to twenty years for building and improvements. Expenditures for maintenance and repairs are charged to expense as incurred, and expenditures for major renewals and improvements are capitalized.

*Impairment of Long-Lived Assets*

We assess the recoverability of long-lived assets for which an indicator of impairment exists. Specifically, we calculate, and recognize, any impairment losses by comparing the carrying value of these assets to our estimate of the undiscounted future operating cash flows. Although our current and historical negative cash flows are indicators of impairment, we believe the future cash flows to be received from our long-lived assets will exceed the assets carrying value. Accordingly, we have not recognized any impairment losses through December 31, 2003.

*Revenue Recognition*

Revenue from collaborative agreements consists of upfront fees, research and development funding, and milestone payments. Non-refundable upfront fees are deferred and amortized to revenue over the related estimated performance period. Periodic payments for research and development activities are recognized over the period in which we perform those activities under the terms of each agreement. Revenue resulting from the achievement of milestone events stipulated in the agreements is recognized when the milestone is achieved.

*Research and Development*

Research and development costs are charged to expense as incurred.

*Income Taxes*

We account for income taxes under the asset and liability method. Deferred tax assets and liabilities are recognized for the future tax consequences attributable to differences between the financial statement carrying amounts of existing assets and liabilities and their respective tax bases and operating loss and tax credit carryforwards. Deferred tax assets and liabilities are measured using enacted tax rates expected to apply to taxable income in the years in which those temporary differences are expected to be recovered or settled. The effect on deferred tax assets and liabilities of a change in tax rates is recognized in income in the period that includes the enactment date.

*Net Loss Per Share*

Basic loss per share is computed by dividing net loss by the weighted-average number of common shares outstanding for the period. Diluted loss per share reflects the potential dilution from the exercise or conversion of securities into common stock. For the years ended December 31, 2001, 2002, and 2003, the effects of the exercise of outstanding stock options were antidilutive; accordingly, they were excluded from the calculation of diluted earnings per share. See Note 10 for a summary of outstanding options.

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**Neose Technologies, Inc.**

(a development-stage company)

**Notes to Financial Statements**

*Comprehensive Loss*

Our comprehensive loss for the years ended December 31, 2001, 2002, and 2003 is comprised only of our net loss, and was $13,329,000, $26,417,000, and $37,681,000, respectively.

*Fair Value of Financial Instruments*

As of December 31, 2003, the carrying values of cash and cash equivalents, restricted funds, accounts receivable, accounts payable, accrued expenses, and accrued compensation approximate their respective fair values. In addition, we believe the carrying value of our debt instruments, which do not have readily ascertainable market values, approximates their fair values.

*Stock-based Compensation*

We apply the intrinsic value method of accounting for all stock-based employee compensation in accordance with APB Opinion No. 25, Accounting for Stock Issued to Employees (APB 25), and related interpretations. We record deferred compensation for option grants to employees for the amount, if any, by which the market price per share exceeds the exercise price per share. In addition, we apply fair value accounting for option grants to non-employees in accordance with Statement of Financial Accounting Standards No. 123, Accounting for Stock-Based Compensation (SFAS No. 123), and Emerging Issues Task Force Issue 96-18, Accounting for Equity Instruments That Are Issued to Other Than Employees for Acquiring, or in Conjunction with Selling, Goods or Services (EITF 96-18).

We have elected to adopt only the disclosure provisions of Statement of Financial Accounting Standards No. 148, Accounting for Stock-Based Compensation Transition and Disclosure, an amendment of FASB Statement No. 123. The following table illustrates the effect on our net loss and basic and diluted net loss per share if we had recorded compensation expense for the estimated fair value of our stock-based employee compensation, consistent with SFAS No. 123 (in thousands, except per share data):

| Year Ended December 31, | 2001 | 2002 | 2003 |
|---|---|---|---|
| Net loss as reported | $ (13,329) | $ (26,417) | $ (37,681) |
| Add: Stock-based employee compensation expense included in reported net loss | 125 | 171 | 100 |
| Deduct: Total stock-based employee compensation expense determined under fair value-based method for all awards | (8,179) | (15,588) | (11,893) |

| | | | | |
|---|---|---|---|---|
| Net loss pro forma | | $ (21,383) | $ (41,834) | $ (49,474) |
| Basic and diluted net loss per share | as reported | $ (0.95) | $ (1.85) | $ (2.14) |
| Basic and diluted net loss per share | pro forma | $ (1.52) | $ (2.94) | $ (2.81) |

*Recent Accounting Pronouncements*

In April 2003, the Financial Accounting Standards Board (FASB) issued Statement of Financial Accounting Standards No. 149, Amendment of Statement 133 on Derivative Instruments and Hedging Activities (SFAS No. 149). This Statement amends and clarifies accounting for derivative instruments, including certain derivative instruments embedded in other contracts, and for hedging activities under SFAS No. 133. SFAS No. 149 was effective for contracts entered into or modified after June 30, 2003, for hedging relationships designated after June 30, 2003, and to certain preexisting contracts. The adoption of SFAS No. 149 did not have an impact on our financial statements.

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**Neose Technologies, Inc.**

(a development-stage company)

**Notes to Financial Statements**

In May 2003, the FASB issued SFAS No. 150, Accounting for Certain Financial Instruments with Characteristics of both Liabilities and Equity . This Statement establishes standards for how an issuer classifies and measures certain financial instruments with characteristics of both liabilities and equity. SFAS No. 150 was effective for financial instruments entered into or modified after May 31, 2003, and is otherwise effective July 1, 2003. The adoption of SFAS No. 150 did not have an impact on our financial statements as we do not have any instruments that are within the scope of this statement.

In December 2003, the FASB issued FASB Interpretation No. 46 (revised December 2003), Consolidation of Variable Interest Entities (FIN 46R), which addresses how a business enterprise should evaluate whether it has a controlling financial interest in an entity through means other than voting rights and accordingly should consolidate the entity. FIN 46R replaces FASB Interpretation No. 46, Consolidation of Variable Interest Entities, which was issued in January 2003. We will be required to apply FIN 46R to variable interests in variable interest entities created after December 31, 2003. We do not have any variable interests in variable interest entities.

*Reclassification*

Certain prior year amounts have been reclassified to conform to our current year presentation.

**Note 3. Supplemental Disclosure of Cash Flow Information**

The following table contains additional cash flow information for the periods reported.

| | Year ended December 31, | | | Period from inception (January 17, 1989) to December 31, 2003 |
|---|---|---|---|---|
| | 2001 | 2002 | 2003 | |
| Supplemental disclosure of cash flow information: | | | | |
| Cash paid for interest | $ 284 | $ 142 | $ 465 | $ 3,910 |
| Non-compete agreement | $ | $ | $ 882 | $ 882 |

| | | | | |
|---|---|---|---|---|
| Non-cash investing activities: | | | | |
| Increase (decrease) in accrued property and equipment | $ 1,525 | $ (1,698) | $ 753 | $ 855 |
| Assets acquired under capital leases | $ | $ 50 | $ 787 | $ 837 |
| Non-cash financing activities: | | | | |
| Issuance of common stock for dividends | $ | $ | $ | $ 90 |
| Issuance of common stock to employees in lieu of cash compensation | $ | $ | $ | $ 44 |

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**Neose Technologies, Inc.**

(a development-stage company)

**Notes to Financial Statements**

**Note 4. Property and Equipment**

Property and equipment consisted of the following (in thousands):

| December 31, | 2002 | 2003 |
|---|---|---|
| Building and improvements | $ 14,872 | $ 27,989 |
| Laboratory and office equipment | 8,964 | 16,024 |
| Land | 700 | 700 |
| Construction-in-progress | 21,440 | 5,217 |
| | 45,976 | 49,930 |
| Less accumulated depreciation | (9,468) | (12,738) |
| | $ 36,508 | $ 37,192 |

The construction-in-progress as of December 31, 2002 represents amounts incurred related to improvements to our owned facility in Horsham, PA. and our leased facility in Horsham, PA. During 2001 and 2002, we incurred $17,448,000 for the construction and validation of our cGMP facility at our existing Horsham location. Our cGMP facility was placed in-service in January 2003. Of the total project cost, $12,488,000 is considered building improvements and will be depreciated over 20 years and $4,960,000 is laboratory equipment and will be depreciated over seven years. Separately, in 2002 we incurred $3,992,000 for the design and renovations of our leased facility in Horsham. Later in 2002, we suspended plans to complete these renovations. In November 2003, we reinitiated renovation activities at an expected additional cost of $6,300,000, which is incremental to the $4,081,000 previously invested in these renovations, on approximately 25,000 square feet of the facility, leaving approximately 15,000 square feet available for future expansion. Our construction-in-progress at December 31, 2002 and 2003 includes $3,992,000 and $5,091,000, respectively, in renovations to this facility.

During the years ended December 31, 2001, 2002, and 2003, we capitalized $70,000, $150,000, and $42,000, respectively, of interest expense in connection with our facility improvement projects. Depreciation expense was $1,825,000, $2,311,000, and $4,047,000 for the years ended December 31, 2001, 2002, and 2003, respectively. During the year ended December 31, 2003, we recorded a loss on disposition of property and equipment of $264,000.

**Note 5. Acquired Intellectual Property**

In 1999, we acquired the carbohydrate-manufacturing patents, licenses, and other intellectual property of Cytel Corporation for aggregate consideration of $4,750,000. The acquired intellectual property consists of core technology with alternative future uses. The acquired intellectual property balance is being amortized to research and development expense in our statements of operations over eight years, which is the estimated useful life of the technology. Amortization expense relating to the acquired intellectual property was $598,000, $598,000, and $597,000, respectively, for each of the years ended December 31, 2001, 2002, and 2003.

**Note 6. Other Assets**

*Investment in Convertible Preferred Stock*

In 2000, we made an investment of $1,250,000 in Series A convertible preferred stock of Neuronyx, Inc., and entered into a research and development collaboration with Neuronyx for the discovery and development of drugs for treating Parkinson s disease and other neurological diseases. The collaboration agreement provides for each of Neose and Neuronyx to perform and fund specific tasks, and to share in any financial benefits of the collaboration. During the year ended December 31, 2003, we did not incur any research and development expense related to this

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**Neose Technologies, Inc.**

(a development-stage company)

**Notes to Financial Statements**

collaboration. We incurred research and development expense related to this collaboration of $1,045,000 and $297,000 during the years ended December 31, 2001 and 2002, respectively. We recorded the equity investment at cost. In October 2003, Neuronyx informed us that they were nearing completion of a Series C equity financing, under which Series C and Series B Neuronyx investors would have an aggregate liquidation preference that is senior to the Series A liquidation preference and exceeds the assumed post-money valuation of Neuronyx. As a result, we reduced the carrying value of our equity investment to zero as of September 30, 2003 by recording a non-cash charge, which is reflected as an impairment of equity securities in our statements of operations.

*Receivable from Related Party*

In 2001, we entered into a tuition reimbursement agreement with an employee who subsequently became an executive officer. Under the agreement, we agreed to lend the amounts necessary to pay for the employee s tuition payments and related costs and fees. Interest accrues on the loan at 4.71% per year, and is payable annually beginning in May 2002. We have agreed to forgive repayment of the principal amount outstanding in four equal, annual installments commencing in May 2004 if the employee remains employed by us on each forgiveness date. We will forgive the accrued interest on its annual due date and, if the employee is terminated without cause, we will forgive all outstanding principal and interest. During 2003, we forgave accrued interest of $8,000. As of December 31, 2002 and 2003, the amounts outstanding under the agreement, including accrued interest, were $121,000 and $118,000, respectively.

**Note 7. Long-Term Debt and Capital Lease Obligations**

Long-term debt and capital lease obligations consisted of the following (in thousands):

| December 31, | 2002 | 2003 |
|---|---|---|
| Industrial development authority bonds | $ 5,100 | $ 3,900 |
| Equipment loans | 2,261 | 6,082 |
| Capital lease obligations | 50 | 619 |
| | 7,411 | 10,601 |
| Less current portion | (1,851) | (2,231) |
| | $ 5,560 | $ 8,370 |

Minimum principal repayments of long-term debt and capital lease obligations as of December 31, 2003 were as follows (in thousands): 2004 $2,231; 2005 $3,335; 2006 $2,436; 2007 $1,328; 2008 $927; and thereafter $344. Because we expect to refinance our Industrial Development Authority bonds during the first quarter of 2004 under a credit agreement entered into in January 2004, we have adjusted the minimum principal repayments relating to the bonds to reflect principal repayment schedule of the new debt. Pursuant to Statement of Financial Accounting Standards No. 6, Classification of Short-Term Obligations Expected to Be Refinanced (SFAS No. 6), short-term obligations, such as the $1,200,000 principal payment due during 2004 under the terms of our taxable Industrial Development Authority bonds, should be excluded from current liabilities if a financing agreement for refinancing of the short-term agreement meets certain criteria. The existing credit agreement with our bank meets the criteria specified in SFAS No. 6. Therefore, we reclassified the $1,200,000 due in 2004 under the terms of the taxable bonds as a long-term liability.

*Credit Agreement*

In January 2004, we borrowed $6,200,000 from a bank for the purpose of funding improvements to our leased facility in Horsham, PA. The credit agreement with our bank provides for us to borrow from the bank an additional $1,800,000 and to utilize $1,100,000 of our restricted cash for the purpose of paying in full the

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**Neose Technologies, Inc.**

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**Notes to Financial Statements**

$2,900,000 outstanding of our taxable Industrial Development Authority bonds, which payment we expect to occur during the first quarter of 2004. During the first quarter of 2004, we expect to enter into another agreement with the bank for it to acquire and reissue the $1,000,000 outstanding of our tax-exempt Industrial Development Authority bonds. If the tax-exempt bond acquisition described above does not occur, the existing credit agreement provides for us to borrow an additional $1,000,000 for the purpose of paying in full the outstanding amount of the tax-exempt Industrial Development Authority bonds.

Initially, the interest rate on the bonds will vary quarterly, depending on LIBOR rates. We will have the option each quarter to incur interest on the outstanding principal at a LIBOR-based variable interest rate or a fixed rate offered by our bank.

If the tax-exempt bond acquisition described above occurs, we will make quarterly, interest-only payments on the related $1,000,000 debt for ten years followed by a single repayment of principal at the end of the ten-year loan period. For the debt outstanding under the existing credit agreement, we will make quarterly, interest-only payments through March 31, 2005. Commencing on March 31, 2005, we will make quarterly principal and interest payments over the remaining nine years of the ten-year loan period. The outstanding debt will be $8,000,000 if the tax-exempt bond acquisition described above occurs and $9,000,000 if the tax-exempt bond acquisition described above does not occur.

To provide credit support for the agreement, we granted a second mortgage to our bank on the land and building where our present headquarters are located, as well as on improvements, certain equipment, and other tangible personal property. The second mortgage will automatically convert to a first mortgage upon payment in full of our Industrial Development Authority Bonds, which payment we expect to occur during the first quarter of 2004. In the credit agreement, we agreed to limit our total outstanding debt to $22,000,000. After using a portion of the proceeds to repay existing debt, our total debt outstanding will be approximately $15,700,000. At any time after the fourth year of the loan period, or if we fail to maintain a minimum required cash and short-term investments balance of at least $22,000,000, our bank has the option to require additional collateral from us in the form of a letter of credit or a security interest in certain cash and short-term investments.

*Industrial Development Authority Bonds*

In 1997, we issued, through the Montgomery County (Pennsylvania) Industrial Development Authority, $9,400,000 of taxable and tax-exempt bonds, of which $3,900,000 was outstanding as of December 31, 2003. As mentioned above, we expect during the first quarter of 2004 to pay in full the outstanding loan balance of the taxable bonds and to have our bank acquire and reissue the tax-exempt bonds.

Pursuant to Statement of Financial Accounting Standards No. 6, Classification of Short-Term Obligations Expected to Be Refinanced (SFAS No. 6), short-term obligations, such as the $1,200,000 principal payment due during 2004 under the terms of our taxable Industrial Development Authority bonds, should be excluded from current liabilities if a financing agreement for refinancing of the short-term agreement meets certain criteria. The existing credit agreement with our bank meets the criteria specified in SFAS No. 6. Therefore, we reclassified the $1,200,000 due in 2004 under the terms of the taxable bonds as a long-term liability.

The bonds are supported by an AA-rated letter of credit, and a reimbursement agreement between our bank and the letter of credit issuer. The interest rate on the bonds varies weekly, depending on market rates for AA-rated taxable and tax-exempt obligations, respectively. During 2001, 2002, and 2003, the weighted-average, effective interest rate was 5.3%, 3.3%, and 2.7% per year, including letter-of-credit and other fees.

The terms of the bond issuance provide for monthly, interest-only payments and a single repayment of principal at the end of the twenty-year life of the bonds. However, under our agreement with our bank, we make monthly payments to an escrow account to provide for an annual prepayment of principal. As of December 31,

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2003, we had restricted funds relating to the taxable bonds of $901,000, which consisted of our monthly payments to an escrow account plus interest earned on the balance of the escrow account. During the first quarter of 2004, we expect to use the restricted funds and a portion of the proceeds under the credit agreement we entered into in January 2004 to pay in full the outstanding loan balance of the taxable bonds.

To provide credit support for this arrangement, we granted a first mortgage on land, building, improvements, and certain equipment to our bank. The net book value of the pledged assets was $20,899,000 as of December 31, 2003. We also agreed to maintain a minimum required cash and short-term investments balance of at least two times the outstanding loan balance. If we fail to comply with this covenant, we are required to deposit with the lender cash collateral up to, but not more than, the unpaid balance of the loan. At December 31, 2003, we were required to maintain $7,800,000 of cash and short-term investments.

*Equipment Loans*

In December 2003, we borrowed $1,201,000 secured by laboratory equipment and facility improvements, which had a book value of $1,207,000 as of December 31, 2003. The terms of the financing require us to pay monthly principal and interest payments over 48 months at an interest rate of 8.66%.

In September 2003, we borrowed $831,000 secured by laboratory equipment and facility improvements, which had a book value of $712,000 as of December 31, 2003. The terms of the financing require us to pay monthly principal and interest payments over 48 months at an interest rate of 8.35%.

In March 2003, we borrowed $2,954,000 secured by laboratory equipment, which had a book value of $2,703,000 as of December 31, 2003. The terms of the financing require us to pay monthly principal and interest payments over 42 months at an annual interest rate of 8.35%.

During 2002, we borrowed $2,261,000 secured by laboratory equipment, which had a book value of $1,868,000 as of December 31, 2003. We are required to make monthly principal and interest payments at an annual interest rate of 8.00% over a three-year period ending January 2006.

*Capital Lease Obligations*

In September 2003, we entered into a capital lease obligation for equipment with a book value of $354,000, which was calculated using an assumed incremental annual borrowing rate of 7.96%. The terms of the lease required us to make an initial payment of $90,000 followed by monthly payments through September 2006. This equipment had an aggregate net book value of $325,000 as of December 31, 2003. We also entered into a capital lease obligation during September 2003 for software with a fair value of $60,000. The terms of the lease require us to make monthly payments through September 2008. As of December 31, 2003, this software had a net book value of $57,000.

During the quarter ended June 30, 2003, we entered into various capital lease obligations for equipment and software with an aggregate book value of $373,000, which was calculated using an assumed incremental annual borrowing rate of 8.35%. We are required to make monthly payments on each lease. The leases have expiration dates ranging from April 2006 to June 2006. As of December 31, 2003, the aggregate net book value of the assets under these leases was $57,000.

In November 2002, we entered into a capital lease obligation for computer equipment that had a book value of $50,000. The lease has an imputed interest rate of 6.2%. We are required to make monthly payments over a three-year period ending November 2005. As of December 31, 2003, this computer equipment had an aggregate net book value of $33,000.

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**Note 8. Accrued Expenses**

Accrued expenses consisted of the following (in thousands):

| December 31, | 2002 | 2003 |
|---|---|---|
| Property and equipment | $ 102 | $ 855 |
| Professional fees | 500 | 444 |
| Employee relocation | 315 | 349 |
| Outside research expenses | 573 | 142 |
| Other expenses | 390 | 643 |
| | $ 1,880 | $ 2,433 |

**Note 9. Stockholders Equity**

*Common Stock*

In September 2003, we sold 2,655,557 shares of common stock in a registered offering to a group of institutional and individual investors at a price of $9.00 per share, generating net proceeds of $22,377,000.

In February 2003, we sold 2,866,763 shares of common stock in a private placement to a group of institutional and individual investors at a price of $6.00 per share, generating net proceeds of $16,320,000.

In March 2000, we offered and sold 2,300,000 shares of our common stock at a public offering price of $32.00 per share. Our net proceeds from the offering after the payment of underwriting fees and offering expenses were $68,605,000.

In June 1999, we sold 1,500,000 shares of common stock in a private placement to a group of institutional and individual investors at a price of $9.50 per share, generating net proceeds of $13,416,000. In January 1999, we sold 286,097 shares of common stock to Johnson & Johnson Development Corporation at a price of $13.98 per share, generating net proceeds of $4,000,000.

In January 1997, we sold 1,250,000 shares of common stock in a public offering at a price of $17.50 per share. Our net proceeds from this offering after the payment of placement fees and offering expenses were $20,339,000.

Our initial public offering closed in February 1996. We sold 2,587,500 shares of common stock, which included the exercise of the underwriters over-allotment option in March 1996, at a price of $12.50 per share. Our net proceeds from this offering after the underwriting discount and payment of offering expenses were $29,127,000. In connection with this offering, all outstanding shares of Series A, C, D, E, and F Convertible Preferred Stock converted into 2,410,702 shares of common stock.

*Shareholder Rights Plan*

In September 1997, we adopted a Shareholder Rights Plan. Under this plan, which was amended in December 1998, holders of common stock are entitled to receive one right for each share of common stock held. Separate rights certificates would be issued and become exercisable if any acquiring party either accumulates or announces an offer to acquire at least 15% of our common stock. Each right will entitle any holder who owns less than 15% of our common stock to buy one one-hundredth share of the Series A Junior Participating Preferred Stock at an exercise price of $150. Each one one-hundredth share of the Series A Junior Participating Preferred Stock is

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essentially equivalent to one share of our common stock. If an acquiring party accumulates at least 15% of our common stock, each right entitles any holder who owns less than 15% of our common stock to purchase for $150 either $300 worth of our common stock or $300 worth of the 15% acquirer s common stock. In November 2000, the Plan was amended to increase the threshold from 15% to 20% for Kopp Investment Advisors, Inc. and related parties. In June 2002 and October 2002, the Plan was amended to increase the threshold to 20% and 25%, respectively, for Eastbourne Capital Management, LLC and related parties. The rights expire in September 2007 and may be redeemed by us at a price of $.01 per right at any time up to ten days after they become exercisable.

**Note 10. Compensation Plans**

*Stock Option Plans*

We have three stock option plans, the 1991, 1992, and 1995 Stock Option Plans, under which a total of 5,876,666 shares of common stock have been reserved. In addition, we granted nonqualified stock options outside of these plans in 1995 to two consultants to purchase an aggregate of 69,998 shares and in 2002 to our Chief Executive Officer and President to purchase 487,520 shares. The 1995 Stock Option Plan, which incorporates the two predecessor plans, provides for the granting of both incentive stock options and nonqualified stock options to our employees, officers, directors, and consultants. In addition, the plan allows us to issue shares of common stock directly either through the immediate purchase of shares or as a bonus tied to either an individual s performance or our attainment of prescribed milestones. Incentive stock options may not be granted at an exercise price less than the fair market value on the date of grant. In addition, the plan includes stock appreciation rights to be granted at our discretion. The stock options are exercisable over a period, which may not exceed ten years from the date of grant, determined by our board of directors. A summary of the status of stock options as of December 31, 2001, 2002, 2003, and changes during each of the years then ended, is presented below:

| | 2001 | | 2002 | | 2003 | |
|---|---|---|---|---|---|---|
| | Number Outstanding | Weighted-Average Exercise Price Per Share | Number Outstanding | Weighted-Average Exercise Price Per Share | Number Outstanding | Weighted-Average Exercise Price Per Share |
| Balance as of January 1 | 2,506,901 | $ 16.61 | 3,112,256 | $ 20.39 | 4,326,869 | $ 19.66 |
| Granted | 789,035 | 32.48 | 1,588,721 | 16.92 | 668,320 | 8.44 |
| Exercised | (79,055) | 11.28 | (209,307) | 7.42 | (62,780) | 2.74 |

| | | | | | | |
|---|---|---|---|---|---|---|
| Canceled | (104,625) | 27.98 | (164,801) | 22.49 | (593,810) | 19.51 |
| Balance as of December 31 | 3,112,256 | $ 20.39 | 4,326,869 | $ 19.66 | 4,338,599 | $ 18.20 |
| Options exercisable as of December 31 | 1,782,271 | $ 14.86 | 2,041,726 | $ 17.86 | 2,420,961 | $ 19.03 |

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The following table summarizes information about stock options outstanding as of December 31, 2003:

| Options Outstanding | | | | | Options Exercisable | |
|---|---|---|---|---|---|---|
| Range of Exercise Prices | Number Outstanding | Weighted-Average Remaining Life (Years) | Weighted-Average Exercise Price | | Number Exercisable | Weighted-Average Exercise Price |
| $ 0.90 $7.32 | 99,389 | 4.4 | $ | 4.38 | 83,189 | $ 3.82 |
| $ 7.45 $10.62 | 1,642,902 | 8.6 | $ | 8.55 | 571,130 | $ 9.11 |
| $11.15 $15.13 | 855,360 | 4.8 | $ | 13.51 | 747,135 | $ 13.79 |
| $15.25 $21.11 | 194,232 | 5.1 | $ | 18.96 | 151,732 | $ 18.57 |
| $23.00 $31.75 | 660,966 | 7.3 | $ | 28.46 | 421,191 | $ 28.41 |
| $32.05 $41.13 | 885,750 | 7.9 | $ | 34.35 | 446,584 | $ 34.63 |
| | 4,338,599 | 7.2 | $ | 18.20 | 2,420,961 | $ 19.03 |

*Fair Value Disclosures*

We have elected to adopt only the disclosure provisions of SFAS No. 123. Accordingly, we apply APB 25 and related interpretations in accounting for our stock-based employee compensation. We record deferred compensation for option grants to employees for the amount, if any, by which the market price per share exceeds the exercise price per share. We amortize deferred compensation over the vesting periods of each option. We recognized $125,000, $171,000, and $100,000 of compensation expense related to employee stock options for the years ended December 31, 2001, 2002, and 2003, respectively. In addition, we recorded $825,000 and $1,608,000 of expense related to the modification of certain stock options to former employees for the years ended December 31, 2001 and 2002. See Note 12 for a description of separation and retirement agreements.

The weighted-average fair value of options granted in 2001, 2002, and 2003 was $22.55, $12.81, and $5.76, respectively. The fair value of each option grant was estimated on the date of grant using the Black-Scholes option-pricing model. We used the following weighted-average assumptions for 2001, 2002, and 2003 grants, respectively: risk-free interest rate of 4.9%, 4.2%, and 3.0%; expected life of 6.1, 6.7, and 5.5 years; volatility of 75%, 80%, and 80%; and a dividend yield of zero. The weighted-average fair value of employee purchase rights granted under our employee stock purchase plan (see below) in 2001, 2002, and 2003 was $11.60, $15.37, and $19.79, respectively. The fair value of the purchase rights was estimated using the Black-Scholes model with the following weighted-average assumptions for 2001, 2002, and 2003,

respectively: risk-free interest rate of 4.6%, 2.9%, and 2.9%; expected life of 16, 17, and 22 months; volatility of 75%, 80%, and 80%; and a dividend yield of zero.

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A summary of options granted at exercise prices equal to, greater than, and less than the market price on the date of grant is presented below:

| Year Ended December 31, | 2001 | 2002 | 2003 |
|---|---|---|---|
| Exercise Price = Market Value | | | |
| Options granted | 610,400 | 1,578,800 | 659,732 |
| Weighted-average exercise price | $ 30.96 | $ 16.98 | $ 8.51 |
| Weighted-average fair value | $ 21.29 | $ 12.79 | $ 5.73 |
| Exercise Price > Market Value | | | |
| Options granted | | | |
| Weighted-average exercise price | $ | $ | $ |
| Weighted-average fair value | $ | $ | $ |
| Exercise Price < Market Value | | | |
| Options granted | 178,635 | 9,921 | 8,588 |
| Weighted-average exercise price | $ 37.67 | $ 6.00 | $ 3.26 |
| Weighted-average fair value | $ 26.85 | $ 15.46 | $ 8.18 |

*Non-employee Stock Options*

During the years ended December 31, 2001 and 2003, we recognized $463,000 and $44,000, respectively, of compensation expense in connection with the vesting of stock options granted to non-employees. During the year ended December 31, 2002, we recognized a gain of $598,000 in connection with the vesting of stock options granted to non-employees. The compensation expense or gain was based on each option s estimated fair value, which was calculated using the Black-Scholes option-pricing model. Because we re-value each option over the related vesting term in accordance with EITF 96-18, increases in our stock price result in increased expense while decreases in our stock price result in a gain. At December 31, 2002, our closing stock price was lower than at December 31, 2001 and, therefore, we recognized a gain during 2002.

*Employee Stock Purchase Plan*

We maintain an employee stock purchase plan, or ESPP, for which 183,000 shares are reserved for issuance. The ESPP allows any eligible employee the opportunity to purchase shares of our common stock through payroll deductions. The ESPP provides for successive, two-year offering periods, each of which contains four semiannual purchase periods. The purchase price at the end of each purchase period is 85% of the lower of the market price per share on the employee s entry date into the offering period or the market price per share on the purchase date. Any employee who owns less than 5% of our common stock may purchase up to the lesser of:

10% of his or her eligible compensation;

1,000 shares per purchase; or

the number of shares per year that does not exceed the quotient of $25,000 divided by the market price per share on the employee s entry date into the offering period.

A total of 42,327 shares of common stock remained available for issuance under the ESPP as of December 31, 2003. The total purchases of common stock under the ESPP during the years ended December 31, 2001, 2002, and 2003, were 17,790 shares at a total purchase price of $335,000, 32,149 shares at a total purchase price of

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$384,000, and 25,836 shares at a total purchase price of $196,000, respectively. We have not recorded any compensation expense for the ESPP. In connection with the employee stock purchases occurring in 2003, we reissued 6,000 shares of treasury stock, which were originally acquired in 2001 for $175,000.

*401(k) Plan*

We maintain a 401(k) Savings Plan (401(k) Plan) for our employees. Employee contributions are voluntary and are determined on an individual basis, with a maximum annual amount equal to the lesser of the maximum amount allowable under federal income tax regulations or 15% of the participant s compensation. We match employee contributions up to specified limits. We contributed $149,000, $176,000, and $216,000 to the 401(k) Plan for the years ended December 31, 2001, 2002, and 2003, respectively.

**Note 11. Revenues from Collaborative Agreements**

Our revenues from collaborative agreements have historically been derived from a few major collaborators. Our collaborative agreements have had some or all of the following elements: upfront fees, research and development funding, milestone revenues, and royalties on product sales.

In November 2003, we entered into two research, development and license agreements with Novo Nordisk A/S to use our GlycoPEGylation technology to develop three next-generation proteins within Novo Nordisk s therapeutic areas, one of which is currently marketed by them. Under the terms of the new agreements, we received a non-refundable, upfront fee of $4,300,000. We deferred the upfront fee, and will amortize this amount over an expected performance period of five years. We will also receive up to $51,300,000 in milestone payments based on the progress of the programs. Novo Nordisk is responsible for funding our research and development activities under the agreements, and we will receive royalties on sales of any products commercialized under the agreements. In addition, we could receive additional milestones and royalties on new indications for the two proteins not currently marketed by Novo Nordisk. During the year ended December 31, 2003, Novo Nordisk accounted for $694,000, or 48%, of our revenues, of which $107,000 represented amortization of the upfront fee. During the quarter ended June 30, 2003, we entered into a license agreement with a company, which accounted for $400,000, or 28%, of our revenues during the year ended December 31, 2003.

During the years ended December 31, 2001, 2002, and 2003, Wyeth accounted for $1,167,000, $4,472,000, and $250,000, respectively, of our collaborative revenues. These amounts represented 92%, 93%, and 17%, of our collaborative revenues during the years ended December 31, 2001, 2002, and 2003, respectively. During 2002, we recognized $3,750,000 related to one of our Wyeth collaborations, which was terminated in September 2002. Of this amount, $1,000,000 was non-cash, and represented the recognition of an upfront fee, which we received from Wyeth in 2001. We deferred the upfront fee, and amortized this amount as revenue over the expected performance period of the related Wyeth agreement. During 2003, we completed activities related to our other Wyeth collaboration, and recorded as revenue the last scheduled payment for research funding of $250,000, which we had received in 2002.

**Note 12. Separation and Retirement Agreements**

In 2002, we entered into a Separation and Consulting Agreement with our former Chief Executive Officer, Stephen A. Roth. Under this agreement, we agreed to provide medical benefits to Dr. Roth and to pay him $39,622 per month for 12 months. During 2002, we recorded severance expense related to this agreement of $309,000, which represented the present value of his future benefit payments.

Prior to March 29, 2003, Dr. Roth had the right to extend his non-competition and non-solicitation commitments for two additional years by entering into a separate non-competition agreement. Dr. Roth extended his commitments in March 2003 and, therefore, we will pay him $39,622 per month for 24 additional months and,

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should he leave our board of directors during the additional two-year period, we will continue his stock option vesting and exercisability. During 2003, we recorded a liability of $882,000, which represented the present value of the future payments, and a corresponding asset for the value of the non-competition commitment. The asset will be amortized to marketing, general and administrative expense on our statements of operations over the two-year term of the agreement. As of December 31, 2003, the present value of remaining minimum payments under this agreement was approximately $528,000.

In 2002, we entered into a retirement agreement with our Vice President, Research. Under the agreement, he terminated his employment effective June 30, 2002. We have committed to pay a retirement benefit over a five-year period. We continued to provide health insurance benefits through December 31, 2003. During 2002, we recorded severance expense related to this agreement of $516,000, which represented the present value of his future retirement benefit and is included in research and development expense on our statements of operations. In addition, we extended the period during which he may exercise his stock options and recorded a non-cash severance charge associated with this option modification of $1,608,000, which is included in research and development expense on our statements of operations.

**Note 13. Other Income**

In 2000, we invested $562,500 in an 8% convertible subordinated debenture, which included a warrant to purchase shares of common stock, issued by Novazyme Pharmaceuticals, Inc. The investment was charged to research and development expense in our statement of operations for 2000 due to uncertainty regarding realizability. In March 2001, Novazyme committed to pay us $1,653,000 million in November 2002 in exchange for restructuring our agreement. In accordance with Statement of Financial Accounting Standards No. 115, Accounting for Certain Investments in Debt and Equity Securities, we did not record the $1,653,000 due to uncertainty regarding the fair value of the note, thereby reducing our cost basis to zero. In September 2001, Genzyme General acquired Novazyme. As a result, we exercised our warrant to purchase shares of Novazyme, converted our debenture into shares of Novazyme, and exchanged our shares of Novazyme for shares of Genzyme. In 2001, we realized a gain on the sale of Genzyme shares of $6,120,000, which was reflected as other income in our statement of operations. Genzyme also assumed Novazyme s obligation to pay us $1,653,000. In 2002, Genzyme paid us $1,653,000, which resulted in the recognition of a gain that was reflected as other income in our statements of operations.

**Note 14. Commitments**

*Leases*

In April 2001, we entered into a lease agreement for approximately 10,000 square feet of laboratory and office space in California. The initial term of the lease ends in March 2006, at which time we have an option to extend the lease for an additional five years. In July 2001, we entered into a lease agreement for approximately 5,000 square feet of office and warehouse space in Pennsylvania. The lease term expires in December 2004. In February 2002, we entered into a lease agreement for approximately 40,000 square feet of laboratory and office space in Pennsylvania.

The initial term of the lease ends in July 2022, at which time we have an option to extend the lease for an additional five years, followed by another option to extend the lease for an additional four and one-half years. Our rental expense for the years ended December 31, 2001, 2002, and 2003 was $248,000, $583,000, and $923,000, respectively. Minimum future annual payments under our operating lease agreements as of December 31, 2003 were as follows (in thousands): 2004 $792; 2005 $763; 2006 $524; 2007 $445; 2008 $454; and thereafter $7,147.

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*License Agreements*

We have entered into agreements with various entities under which we have been granted licenses to use patent rights and technology. Typically, these agreements will terminate upon the expiration of the applicable patent rights, and require us to reimburse the licensor for fees related to the acquisition and maintenance of the patents licensed to us. In addition, we usually are required to pay royalties to the licensor based either on sales of applicable products by us or specified license fees, milestone fees, and royalties received by us from sublicensees, or both.

**Note 15. Income Taxes**

As of December 31, 2003, we had net operating loss carryforwards for federal and state income tax purposes of approximately $44,638,000 and $8,810,000, respectively. In addition, we had federal research and development credit carryforwards of approximately $4,236,000. All of these carryforwards begin to expire in 2005. Approximately $9,428,000 of the federal net operating loss carryforwards result from tax deductions related to equity-based compensation, which is considered a capital contribution, and not a tax benefit, for financial reporting purposes. Due to the uncertainty surrounding the realization of the tax benefit associated with our federal and state carryforwards, we have provided a full valuation allowance against these tax benefits. In addition, pursuant to the Tax Reform Act of 1986, the annual utilization of our net operating loss carryforwards will be limited. We do not believe that these limitations will have a material adverse impact on the utilization of our net operating loss carryforwards. The approximate income tax effect of each type of carryforward and temporary difference is as follows (in thousands):

| December 31, | 2002 | 2003 |
|---|---|---|
| Benefit of net operating loss carryforwards | $ 1,388 | $ 12,230 |
| Research and development credit carryforwards | 3,217 | 4,236 |
| Capitalized research and development | 17,796 | 22,063 |
| Start-up costs | 15,827 | 13,617 |
| Depreciation and amortization | 5,410 | 5,789 |
| Deferred compensation | 1,978 | |
| Accrued expenses not currently deductible | 534 | 864 |
| Deferred revenue | 102 | 1,702 |
| | 46,252 | 60,501 |
| Valuation allowance | (46,252) | (60,501) |
| | $ | $ |

**Note 16. Related-Party Transaction**

We have a joint venture with McNeil Nutritionals to develop bulking agents for use in the food industry. We account for our investment in the joint venture under the equity method, under which we recognize our share of the income and losses of the joint venture. In 1999, we reduced the carrying value of our initial investment in the joint venture of $345,000 to zero to reflect our share of the joint venture s losses. We recorded this amount as research and development expense in our statement of operations. We will record our share of post-1999 losses of the joint venture only to the extent of our actual or committed investment in the joint venture.

The joint venture developed a process for making fructooligosaccharides and constructed a pilot facility in Athens, Georgia. In 2001, the joint venture closed the pilot facility and is exploring establishing a manufacturing arrangement with a third party to produce this or other bulking agents. As a result, we do not intend to commit the joint venture to make any further investments in facilities.

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For the year ended December 31, 2003, the joint venture had a net loss and a loss from continuing operations of $68,000. The joint venture had no revenues during 2003. As of December 31, 2003, the joint venture had no assets, $150,000 of current liabilities, and $8,580,000 of noncurrent liabilities, which consisted of amounts owed to McNeil Nutritionals.

During the years ended December 31, 2001, 2002, and 2003, we incurred expenses related to the joint venture of $779,000, $252,000, and $21,000, respectively, which were reimbursed to us by the joint venture. These amounts have been reflected as a reduction of research and development expense in our statements of operations. As of December 31, 2003, the joint venture owed us $10,000.

If the joint venture becomes profitable, we will recognize our share of the joint venture s profits only after the amount of our capital contributions to the joint venture is equivalent to our share of the joint venture s accumulated losses. As of December 31, 2003, the joint venture had an accumulated loss since inception of $10,225,000. Until the joint venture is profitable, McNeil Nutritionals is required to fund, as a non-recourse, no-interest loan to the joint venture, all of the joint venture s aggregate capital expenditures in excess of an agreed-upon amount, and all of the joint venture s operating losses. The loan balance would be repayable by the joint venture to McNeil Nutritionals over a seven-year period commencing on the earlier of September 30, 2006 or the date on which Neose attains a 50% ownership interest in the joint venture after having had a lesser ownership interest. In the event of any dissolution of the joint venture, the loan balance would be payable to McNeil Nutritionals by the joint venture before any distribution of assets to us. As of December 31, 2003, the joint venture owed McNeil Nutritionals $8,580,000.

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| Exhibit | Description |
|---|---|
| 10.39*# | Research, Development and License Agreement between Neose Technologies, Inc. and Novo Nordisk A/S dated as of November 17, 2003. |
| 10.40*# | Research, Development and License Agreement among Neose Technologies, Inc. and Novo Nordisk A/S and Novo Nordisk Health Care AG dated as of November 17, 2003. |
| 10.41*# | Amendment to Research, Development and License Agreement between Neose Technologies, Inc. and Novo Nordisk A/S dated December 18, 2003. |
| 10.42*# | Amendment to Research, Development and License Agreement among Neose Technologies, Inc. and Novo Nordisk A/S and Novo Nordisk Health Care AG dated December 18, 2003. |
| 10.43* | Promissory Note of Neose Technologies, Inc. to General Electric Capital Corporation, dated December 18, 2003. |
| 10.44* | Credit Agreement by and between Brown Brothers Harriman & Co. and Neose Technologies, Inc., dated as of January 30, 2004. |
| 10.45* | General Security Agreement by Neose Technologies, Inc. to Brown Brothers Harriman & Co., dated as of January 30, 2004. |
| 10.46* | Open-end Mortgage and Security Agreement by and between Neose Technologies, Inc. and Brown Brothers Harriman & Co., dated as of January 30, 2004. |
| 10.47* | Term Loan Note of Neose Technologies, Inc. to Brown Brothers Harriman & Co., dated January 30, 2004. |
| 23.1* | Consent of KPMG LLP. |
| 23.2* | Information Regarding Consent of Arthur Andersen LLP. |
| 24* | Powers of Attorney (included as part of signature page hereof). |
| 31.1* | Certification by Chief Executive Officer pursuant to Rule 13a-14(a) and 15d-14(a), as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002. |
| 31.2* | Certification by Chief Financial Officer pursuant to Rule 13-14(a) and 15d-14(a), as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002. |
| 32.1* | Certification Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002. |
| 32.2* | Certification Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002. |
| * | Filed herewith. |
| # | Portions of this Exhibit were omitted and filed separately with the Secretary of the SEC pursuant to a request for confidential treatment that has been filed with the SEC. |