NEOSE TECHNOLOGIES INC
Form 10-K
March 08, 2006

UNITED STATES SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549
FORM 10-K

(Mark One)

þ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(D) OF THE SECURITIES EXCHANGE ACT OF 1934**
for the fiscal year ended December 31, 2005 or

o **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**

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)

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes o No þ

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes o No þ

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 þ No o

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 or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. þ

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, or a non-accelerated filer. See definition of accelerated filer and large accelerated filer in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer o Accelerated filer þ Non-accelerated filer o

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Act). Yes o No þ

As of June 30, 2005, the aggregate market value of the registrant s Common Stock held by non-affiliates of the registrant was approximately $68,770,104 based on the last sale price of the Common Stock on such date as reported by The NASDAQ National Market. This calculation excludes 10,950,593 shares held on June 30, 2005 by directors, executive officers, and two holders of more than 10% of the registrant s Common Stock.

As of March 3, 2006, there were 32,782,372 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 4, 2006, 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.

PART I

ITEM 1. BUSINESS.

Overview

We are a biopharmaceutical company using our enzymatic technologies to develop proprietary drugs, focusing primarily on therapeutic proteins. We believe that our core enzymatic technologies, GlycoAdvance® and GlycoPEGylation , improve the drug properties of therapeutic proteins by building out, and attaching polyethylene glycol (PEG) to, carbohydrate structures on the proteins. We are using our technologies to develop proprietary versions of protein drugs with proven safety and efficacy and to improve the therapeutic profiles of proteins being developed by our partners. We expect these modified proteins to offer significant advantages, including less frequent dosing and possibly improved efficacy, over the original versions of the drugs now on the market, as well as to meet or exceed the pharmacokinetic profile of next-generation versions of the drugs now on the market. We believe this strategy of targeting drugs with proven safety and efficacy allows us to lower the risk profile of our proprietary development portfolio as compared to *de novo* protein drug development.

Our proprietary drug development portfolio currently consists of two therapeutic protein candidates. GlycoPEG-EPO (NE-180) is a long-acting version of erythropoietin (EPO) produced in insect cells. EPO is prescribed to stimulate production of red blood cells, and is approved for sale in major markets around the world for treatment of chemotherapy-induced anemia and anemia associated with chronic renal failure. In February 2006, we initiated a Phase I clinical trial for NE-180 in a Western European country. We expect this clinical trial to conclude by mid-2006. In the U.S., our Investigational New Drug application (IND) for NE-180 is currently on clinical hold with the U.S. Food and Drug Administration (FDA). We anticipate finalizing our Complete Response to the FDA in early 2006. The timing of submission of this response to the FDA will depend upon the evolution of our regulatory and clinical strategy. The early clinical development of NE-180 could be carried out entirely in Europe. Our second proprietary protein, GlycoPEG-GCSF, is a long-acting version of granulocyte colony stimulating factor (G-CSF) that we are co-developing with BioGeneriX AG, a company of the ratiopharm Group. 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 myelosuppressive chemotherapy. We expect that by the end of the first quarter of 2006, in collaboration with our partner, BioGeneriX, we will commence the regulatory process in a European country. In 2004, the EPO and G-CSF drug categories had aggregate worldwide sales of approximately $10.6 billion and $3.3 billion, respectively.

Opportunities in the Therapeutic Protein Market

Worldwide sales of protein drugs in 2003 have been reported at over $39 billion, and by some estimates are expected to grow to over $70 billion by 2008. We believe that 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 technologies can be applied to many of these marketed drugs to create products with improved clinical profiles. We are pursuing opportunities in this field through our own proprietary drug development portfolio, our exploratory research program and our partnering and licensing program.

Our Technology

Our GlycoAdvance and GlycoPEGylation technologies involve the use of enzymes to modify or initiate, and attach PEG to, carbohydrate structures on glycoproteins (proteins with carbohydrate structures attached). We have developed a special expertise and extensive 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 allow us to create new intellectual property relating to our core technologies as well as new compositions of matter. 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 technologies have broad application to protein drug development and can be extended to provide an opportunity for sustainable growth. We

are using our GlycoAdvance and GlycoPEGylation technologies in our proprietary drug development portfolio, in our exploratory research program and in our partnering and licensing program.

GlycoAdvance. Our GlycoAdvance technology employs enzymes to modify or initiate carbohydrate structures on proteins. Currently, recombinant glycoprotein drugs are often produced in mammalian cell culture expression systems, primarily Chinese hamster ovary (CHO) cells. Generally, carbohydrates are added to 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, thus compromising the half-life and effectiveness of these proteins. Conventional approaches to improving the glycosylation of recombinant protein drugs, such as changing the cell line used for expression, re-engineering the protein, and modifying cell culture conditions or media, are time consuming and frequently provide only partial solutions. In addition, when a protein is inconsistently glycosylated, additional purification may be required to remove incompletely glycosylated drug molecules from the desired drug product, resulting in lower manufacturing yields and increased expense.

Our GlycoAdvance technology addresses these problems by employing enzymes to modify the carbohydrate structures on proteins that have inadequate carbohydrate structures and to initiate carbohydrate structures on proteins that have none. Proteins may have inadequate carbohydrate structures as a result of the cell expression systems used, or may have no carbohydrate structures in their native state or as a result of the cell expression system used. Our GlycoAdvance technology enables the use of alternate expression systems to produce protein drugs, including not only CHO and E. coli, but also insect cells. By modifying or initiating carbohydrate structures on proteins, GlycoAdvance also enables the application of our GlycoPEGylation technology to these proteins.

GlycoPEGylation. Our GlycoPEGylation technology employs enzymes to attach PEG selectively to the carbohydrate structures on glycoprotein drugs, rather than attaching PEG directly to the protein backbone.

Common protein drug delivery problems include poor solubility and stability, proteolysis (rapid degradation), 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, PEG, directly to the amino acid backbone of the protein. Pegylation has been used in marketed drugs, such as PEG-INTRON®, PEGASYS® and Neulasta®. 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.

By employing GlycoAdvance and GlycoPEGylation, we are able to attach PEG efficiently and selectively. By 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. We believe that significant clinical benefits may be achieved through the application of our GlycoPEGylation technology to proteins. By using our GlycoPEGylation technology, we have been able to demonstrate with several drug candidates a prolonged drug effect in animals.

Proprietary Drug Development Portfolio

Our proprietary drug development portfolio currently consists of two next-generation therapeutic protein candidates: a long-acting version of EPO (NE-180) and a long-acting version of G-CSF (GlycoPEG-GCSF).

NE-180. We are developing NE-180, a long-acting version of EPO that is produced in insect cells. We filed for authorization to commence a Phase I clinical trial in a Western European country during the later part of 2005. On January 3, 2006, NE-180 was cleared to proceed into a Phase I clinical trial in this European country, which was initiated in February, 2006. We expect to conclude this Phase I clinical trial for NE-180 by mid-2006.

In the U.S., we submitted an IND for NE-180 to the FDA during the second quarter of 2005. In August 2005, the FDA advised us that it requires additional manufacturing and preclinical information in order to complete its review of the IND and that our proposed Phase I clinical trial of NE-180 in the U.S. had been placed on hold. We anticipate finalizing our Complete Response to the FDA in early 2006. The timing of submission of this response to the FDA will depend upon the evolution of our regulatory and clinical strategy. The early clinical development of NE-180 may be carried out entirely in Europe.

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 chemotherapy-induced anemia and anemia associated with chronic renal failure. EPO accounts for more sales worldwide than any other glycoprotein drug. Worldwide sales in the EPO category in 2004 were approximately $10.6 billion. Of these sales, approximately $7.5 billion were in the U.S., approximately $1.7 billion were in Europe, and approximately $1 billion were in Japan.

Based on preclinical studies, 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 carbohydrate attachment sites and the molecular weight of the PEG that we attach to the compound. In these early animal studies, multiple constructs of GlycoPEGylated EPO, including NE-180, had improved pharmacokinetic and pharmacodynamic profiles as compared with unmodified EPO, and pharmacokinetic and pharmacodynamic profiles comparable to those of Aranesp®, Amgen s long-acting EPO analog. Based on our preliminary market research, we believe that clinicians, particularly oncologists, would respond favorably to a long-acting EPO. This is supported by reported sales data for Aranesp, indicating cumulative sales of approximately $7.7 billion during the period from its launch in 2001 through the fourth quarter of 2005.

We believe that the expiration of key patents covering EPO will provide commercial opportunities in time frames consistent with our development timeline. While we expect to pursue early entry opportunities in the U.S., we plan to pursue regulatory and marketing approval first in Europe, where, the key patents, along with those in Japan, expired in 2005.

In the U.S., we believe that the key patents surrounding EPO expressed in non-vertebrate systems will expire by the end of 2013, and that the remaining key patents will expire by the end of 2015. Accordingly, we believe that our use of an insect cell expression system will allow NE-180 to enter the U.S. market sooner than EPO products expressed in vertebrate or mammalian cells. In addition, we believe that the use of an insect cell expression system may allow us to enter the U.S. market before even the non-vertebrate patents expire. Some of the issues relevant to the analysis of our freedom to operate in the U.S. are the subject of ongoing litigation between other parties. We continue to monitor these matters, as well as evaluate whether the applicable patent claims would block our entry into the U.S. market prior to expiration. In the meantime, we expect to continue development in the U.S. of NE-180 under the protection of a statutory safe harbor.

GlycoPEG-GCSF. We are developing GlycoPEG-GCSF, a long-acting version of G-CSF, in collaboration with our partner BioGeneriX. We expect that by the end of the first quarter of 2006 we and BioGeneriX will commence the regulatory process in a European country. 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 myelosuppressive chemotherapy. Worldwide sales in the G-CSF category in 2004 were approximately $3.3 billion. Of these sales, approximately $2.2 billion were in the U.S., approximately $0.7 billion were in Europe, and approximately $0.4 billion were in Japan.

Based on proof-of-concept data and preclinical development activities, we believe it is feasible to develop a long-acting G-CSF through GlycoPEGylation. These studies suggest that the pharmacokinetic profile of G-CSF can be adjusted by manipulating the number of carbohydrate attachment sites and the molecular weight of the PEG that we attach to the compound. In these early animal studies, multiple constructs of GlycoPEGylated G-CSF, including GlycoPEG-GCSF, had improved pharmacokinetic and pharmacodynamic profiles as compared with unmodified G-CSF (Neupogen®), and pharmacokinetic and pharmacodynamic profiles comparable to those of Neulasta®, Amgen s long-acting G-CSF analog. We believe that clinicians would respond favorably to a long-acting G-CSF as supported by reported sales data for Neulasta, indicating cumulative sales of approximately $5.7 billion during the period from its launch in 2002 through the fourth quarter of 2005.

We believe that the expiration of key patents covering G-CSF will provide commercial opportunities in a time frame consistent with our development timeline. We expect that regulatory approval for GlycoPEG-GCSF will be sought both in and outside the U.S. We believe that key patents covering G-CSF will expire in Europe in 2006, in the U.S. in late 2013 and in other jurisdictions between these times. We expect to pursue regulatory and marketing approval for GlycoPEG-GCSF first in Europe.

Exploratory Research Program

We conduct exploratory research, both independently and with collaborators, on therapeutic candidates, primarily proteins, using our enzymatic technologies. Successful therapeutic candidates may be advanced for development through our own proprietary drug development program, our partnering and licensing program, or a combination of the two. Although our primary focus is the development of long-acting proteins, we are also conducting research to assess opportunities to use our enzymatic technologies in other areas, such as glycopeptides and glycolipids.

Partnering And Licensing Program

Currently we have the following collaborations:

BioGeneriX GlycoPEG-GCSF. In April 2004, we entered into an agreement with BioGeneriX to use our proprietary GlycoAdvance and GlycoPEGylation technologies to develop a long-acting version of G-CSF. Under the agreement, we and BioGeneriX share the expenses of preclinical development, BioGeneriX is responsible for supplying the protein and funding the entire clinical development program and we will be responsible for supplying enzyme reagents and sugar nucleotides. If we and BioGeneriX proceed to commercialization, we will have commercial rights in the U.S., Canada, Mexico and Japan, and BioGeneriX will have commercial rights in Europe and the rest of the world. Each company has the ability to search for its own marketing partner for its territories and will receive significant royalties on product sales in the other company s territory. In connection with the agreement, we received an upfront fee from BioGeneriX. BioGeneriX has the right to terminate the agreement without cause following the completion of preclinical development, in which case we will have all rights to the product candidate, including supply of protein from BioGeneriX or its contract manufacturer. Each party has the right, in various circumstances, to terminate the agreement by giving the required notice to the other party, subject to the other party s right to continue working on the development and commercialization of a long-acting version of G-CSF, as provided in the agreement.

BioGeneriX Additional GlycoPEGylated Protein. On April 28, 2005, we entered into a research, co-development and commercialization agreement with BioGeneriX. We received a non-refundable payment in connection with the execution of this agreement. In addition, under the agreement we are entitled to receive research payments and could receive milestone payments totaling up to $61.5 million, as well as significant royalties on product sales. The agreement provides for us to conduct research on behalf of BioGeneriX for up to 12 months and grant BioGeneriX the right to obtain an exclusive, worldwide license to use our enzymatic technologies to develop and commercialize a long-acting version of the target protein. If BioGeneriX exercises its right to obtain the license, they will be responsible for the further development and commercialization of the target protein. If requested by BioGeneriX, we will provide, and be fully reimbursed for, any required technical assistance. BioGeneriX has the right to terminate the agreement any time after the research period. We have the right to terminate the agreement if specific development milestones are not met within certain periods of time.

Novo Nordisk. In 2003, we entered into agreements with Novo Nordisk A/S to use our GlycoAdvance and GlycoPEGylation technologies to develop and commercialize three next-generation versions of currently-marketed proteins, one of which is marketed by Novo Nordisk. Under these agreements, we received a $4.3 million upfront fee, and Novo Nordisk funds our research and development activities for these three proteins. We may also receive up to $52.2 million in development milestones under these agreements, as amended, as well as significant royalties on sales of the licensed products. Under these agreements, Novo Nordisk s license with respect to each protein continues 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. 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, subject to Novo Nordisk s ability to extend by paying minimum royalties.

MacroGenics. In 2004, we entered into a research collaboration agreement with MacroGenics, Inc. to use our GlycoAdvance and GlycoPEGylation technologies on multiple monoclonal antibodies of MacroGenics, with the goal of improving the therapeutic profiles of these proteins. Under this agreement, MacroGenics has the right to take a limited number of modified compounds into development. During the research phase, we and MacroGenics each fund our own expenses. If MacroGenics decides to proceed with any of the modified compounds beyond the initial research phase, MacroGenics will be responsible for all further development of the licensed compounds and we will receive royalties on any product sales.

Business Strategy

Our primary focus is to develop proprietary protein drugs with proven safety and efficacy, and to improve the therapeutic profiles of glycoproteins being developed by our partners. We may also develop other therapeutic drugs by applying our enzymatic technologies in other areas, such as glycopeptides and glycolipids. Key elements of our strategy are to:

Continue to develop our two long-acting therapeutic protein candidates. We continue to develop our two long-acting proprietary therapeutic protein candidates: NE-180 and GlycoPEG-GCSF. With regard to NE-180, we expect to complete a Phase I clinical trial in a Western European country in mid-2006, and assuming the successful outcome of our Phase I clinical trial in Europe, we may seek to conduct our Phase II clinical trials in Europe in the latter half of 2006. In the U.S., we anticipate finalizing our Complete Response to the FDA in early 2006. The timing of submission of this response to the FDA will depend upon the evolution of our regulatory and clinical strategy. With regard to GlycoPEG-GCSF, we expect that by the end of the first quarter of 2006, in collaboration with our partner, BioGeneriX, we will commence the regulatory process in a European country.

Target drugs with proven safety and efficacy. We are developing improved therapeutics with a current focus on therapeutic proteins using our proprietary enzymatic technologies, GlycoAdvance and GlycoPEGylation. We expect these modified proteins to offer significant advantages, including less frequent dosing and possibly improved efficacy, over the original versions of the drugs now on the market, as well as to meet or exceed the pharmacokinetic and pharmacodynamic profiles of next-generation versions of the drugs now on the market. We believe this strategy of targeting the many commercially attractive protein drugs with proven safety and efficacy allows us to lower the risk profile of our proprietary drug development portfolio as compared to *de novo* protein drug development. We intend to continue to focus our research and development resources on therapeutic proteins that we believe have the highest probability of clinically meaningful therapeutic profile improvements from our technology and are in commercially attractive categories.

Leverage our core competencies. We believe that our core enzymatic technologies improve the drug properties of therapeutic proteins. We will continue to use our technologies to research and develop improved versions of protein drugs with proven safety and efficacy and to improve the therapeutic profiles of glycoproteins being developed by our partners. We will also continue to conduct exploratory drug development research in novel therapeutic categories, such as glycolipids, where our proprietary enzymatic technology, intellectual property and internal expertise provide us with opportunities.

Continue to seek attractive partnership opportunities. We will continue our efforts to build a portfolio of commercially attractive partnerships in a blend of co-developments and licenses. Where possible, we will seek partnerships that allow us to participate significantly in the commercial success of each of the compounds.

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. In connection with our proprietary protein drug program,

we have devoted significant resources to 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 applications, 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 have obtained and continue to seek 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 25 issued U.S. patents, and have licensed 63 issued U.S. patents from 12 institutions. In addition, we own or have licensed over 131 patent applications pending in the U.S. There are also 520 foreign patent applications pending or granted related to our owned and licensed patents. In addition, we have assigned four issued U.S. patents and seven granted or pending foreign counterparts to Magnolia Nutritionals, our joint venture with McNeil Nutritionals (a subsidiary of Johnson & Johnson).

We recently received a Notice of Allowance from the U.S. Patent and Trademark Office for a pending patent application related to our GlycoPEGylation technology. The allowed U.S. claims contained in the application broadly cover glycosyl-linked poly(ethylene glycol) conjugates of therapeutic peptides. This was the first allowed patent application in a series of pending patent applications directed toward our broad GlycoConjugation technology platform.

Proprietary Protein Drugs. To pursue our strategy of developing proprietary protein drugs, we must ascertain the nature, scope and expiration of existing patent claims covering the 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 issued patents or 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.

In order to market proprietary versions of currently marketed proteins, it is necessary to determine the expiration dates of existing patent claims that could cover a 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 in the U.S. and Europe has encouraged us that there may be opportunities to enter the U.S. market sooner than our competitors whose products would have different characteristics or manufacturing processes. If we pursue a strategy of early entry in the U.S., 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 by us, or made known by us 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 us if they are the result of tasks assigned by us or the use of property (including intellectual property) owned or used by us. Our agreements with consultants generally provide that inventions conceived by the consultant while rendering consulting services to us 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.

Others may claim that our technology infringes on their patents. Even if successful, the process of defending against such claims could result in substantial costs and delay our ability to commercialize our product candidates that utilize the challenged technology.

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 FDA and by comparable regulatory agencies in other countries. 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.

After laboratory analysis and preclinical testing in animals, a regulatory filing is required to be submitted to the appropriate authorities before human testing may begin. In the U.S., an IND filing is made to the FDA. In Europe, an Investigational Medicinal Product Dossier (IMPD) or equivalent filing is submitted to the national health authority (Competent Authority) in each country in which a clinical trial is planned. 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 (IRB) in the U.S, or Independent Ethics Committee (IEC) in Europe. During Phase I, small clinical trials are conducted to determine the safety of the product in healthy volunteers. During Phase II, clinical trials are expanded in size and are conducted to assess safety, establish an acceptable dose, and gain preliminary evidence of the efficacy of the product in a subset of the target population. During Phase III, clinical trials are further expanded in size and conducted to obtain sufficient data to establish statistically significant proof of safety and efficacy in the target population. 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 appropriate authority in the form of a Biologics License Application (BLA), or New Drug Application (NDA), both in the U.S., or a Marketing Authorization Application (MAA) or equivalent, in Europe. If the application contains all pertinent information and data, the appropriate regulatory authority will formally accept the file for review. In responding to this filing, the regulatory authority 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 either the U.S. or Europe until an appropriate marketing application has been approved by the responsible regulatory authority(ies). Even after initial regulatory approval is obtained, further clinical trials may be required to provide additional data on safety and effectiveness or 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 Europe (including the European country in which we are conducting a Phase I clinical trial for NE-180) are similar to those in the U.S. The European clinical trials are being performed in a manner consistent with FDA requirements, which would potentially allow the data generated from the European trials to be used to support a U.S. IND application.

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, such as the suspension of our manufacturing operations, the seizure of products we produce, and the suspension of sales of our products.

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 European countries that are members of 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 enter into agreements with third parties for the manufacture of enzymes, sugar nucleotides and other reagents that are used in the production of next-generation glycoPEGylated protein therapeutics using our technology. Any third parties we contract with will be subject to substantially the same regulatory requirements as we are with regard to the items they manufacture for us.

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.

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. A number of these competitors are working on the development of next-generation protein therapeutics. Some of these competitors include Maxygen, Nektar Therapeutics, BioRexis, Human Genome Sciences 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, Roche, Shire, Maxygen, Fibrogen, Affymax and Syntonix. Other companies are active in this area, and we expect that competition will increase. We are also aware that there are several companies engaged in glycobiology research. 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 $3.3 billion during 2005. Roche is developing an improved EPO known as CERA (Continuous Erythropoiesis Receptor Activator). In December 2005, Roche announced that Phase III clinical trials for CERA had been completed and that in 2006 it intends to seek regulatory approval for the limited commercialization of CERA worldwide for certain renal indications. Roche has indicated that it may delay seeking regulatory approval for other indications for up to two years. In addition, in late 2005 Amgen filed a lawsuit against Roche alleging that CERA infringes on Amgen s patents. Besides Amgen and Roche, non-originator companies are applying their technologies to develop improved EPO compounds, such as: Syntonix, with its EPO-Fc fusion protein (which we believe is currently in preclinical development); Fibrogen, with its small molecule promoter of endogenous EPO (which we believe is currently in Phase II); and Affymax, with its synthetic EPO-like peptides (which we believe is currently in Phase II).

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 $2.3 billion for the year ended December 31, 2005. Other companies, such as Maxygen and Affymax, are also applying their technologies to develop long acting competitors to G-CSF (we believe that both of these products are in preclinical development).

Follow-on Biologics (Biogenerics). Several companies are pursuing the opportunity to develop and commercialize follow-on versions of currently marketed biologic products, including EPO, G-CSF and others. These companies include Novartis (Sandoz), BioGeneriX, Stada (Bioceuticals), BioPartners and SICOR (a subsidiary of Teva Pharmaceutical USA). In the U.S. and Japan, a clear development and regulatory path does not currently exist for biologic products that are, or soon will be, off-patent. In Europe, the first guidelines regarding the quality, preclinical and clinical development of follow-on biologics was adopted in September 2005, with additional guidelines expected to be adopted in 2006.

Research and Development Services. Although we are focused on the development of proprietary protein drugs, 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 may compete with efforts within these companies to improve therapeutic protein profiles and expression, and with services provided by other companies to improve proteins, such as chemical pegylation technology.

There are several companies 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, GlycoFi and Momenta. Crucell has developed human cell lines for glycoprotein production. GlycoFi is focused on expressing glycoproteins in yeast systems and Momenta is utilizing sophisticated analysis and design for carbohydrate-based therapeutics.

Manufacturing

We have used our pilot facility to develop manufacturing processes for NE-180, enzyme reagents and key sugar nucleotides (including our sugar-PEG nucleotides). We manufactured NE-180 in sufficient quantities to meet the needs of our expected preclinical and early clinical studies. We plan to transfer the manufacturing process for NE-180 to a third-party contract manufacturer or partner outside of the US for Phase III and commercial supplies.

Our partners currently manufacture the native proteins that are subsequently remodeled using GlycoAdvance and GlycoPEGylation and will incorporate the remodeling processes at their facilities. Our supply chain obligations, outside of NE-180, are therefore confined to the supply of enzyme reagents and sugar nucleotides. We intend to use contract manufacturing organizations (CMOs) for the supply of our enzyme reagents and sugar nucleotides, except those that are available commercially.

Since we now have excess manufacturing capacity, we continue to evaluate alternatives for the disposition of the facility that contains our pilot manufacturing plant.

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, 2005, we employed 109 individuals, consisting of 83 employees engaged in research, development and manufacturing activities, and 26 employees devoted to corporate and administrative activities. Our scientific staff includes carbohydrate biochemists as well as scientists with expertise in organic chemistry, analytical chemistry, molecular biology, microbiology, cell biology, scale-up manufacture, and regulatory affairs. 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.

Upon the completion of the restructuring announced in August 2005, we reduced the size of our workforce by approximately 25% compared to the end of the first quarter of 2005.

Restructuring

In August 2005, we implemented a restructuring of operations to enable an enhanced focus on next-generation proteins, to allow for the anticipated transfer of production of proteins and reagents to our collaborative partners and contract manufacturers now that our programs are more mature, and to reduce cash burn. Upon completion of the restructuring, we reduced the size of our workforce by approximately 25% compared to the end of the first quarter of 2005. Our net loss for 2005 included $14.2 million of charges related to this restructuring, including $13.2 million of non-cash property and equipment impairment charges, most of which related to our Witmer Road facility and related equipment, and $1.0 million of payments for employee severance and facility closure costs.

Internet Address and Securities Exchange Act Filings

Our internet address is www.neose.com. We make available free of charge 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 1A. RISK FACTORS.

Financial Risks

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 cash equivalents, expected revenue from collaborations and license arrangements, and interest income should be sufficient to meet our operating and capital requirements at least through 2006, although changes in our collaborative relationships or our business, whether or not initiated by us, may affect the rate at which we deplete our cash and cash equivalents. Our present and future capital requirements depend on many factors, including:

level of research and development investment required to develop our therapeutic proteins, and maintain and improve our technology position;

the costs of procuring proteins and reagents for research and development and at commercial scale;

the results of preclinical and clinical testing, which can be unpredictable in drug development;

changes in product candidate development plans needed to address any difficulties that may arise in manufacturing, preclinical activities, clinical studies or commercialization;

our ability and willingness to enter into new agreements with collaborators and to extend or maintain our existing collaborations, and the terms of these agreements;

our success rate and that of our collaborators in preclinical and clinical efforts associated with milestones and royalties;

the costs of investigating patents that might block us from developing potential drug candidates;

the costs of recruiting and retaining qualified personnel;

the time and costs involved in obtaining regulatory approvals;

the timing, willingness, and ability of our collaborators to commercialize products incorporating our technologies;

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

the evolution of the competitive landscape.

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 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, preference and 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 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 and technologies, and otherwise respond to competitive pressures could be significantly delayed or limited, and we may need to downsize or halt our operations.

Our debt obligations include restrictive covenants which may restrict our operations or otherwise adversely affect us.

We have a credit facility, which was amended in February 2006, with a bank consisting of a credit agreement and a financing agreement. As of December 31, 2005, the outstanding balance under the credit facility was $8.1 million. Pursuant to the agreements comprising the credit facility, we agreed to limit our total outstanding debt to $22.0 million; therefore, we cannot exceed this limit without the bank s consent. As of December 31, 2005, our total outstanding debt was $14.5 million. The limit on our total debt under the credit agreement could adversely affect us by reducing our flexibility in planning for, or reacting to, changes in our business and our industry.

If the bank determines a material adverse change has occurred in our business, financial condition, results of operations, or business prospects, the bank, in its sole discretion, may declare at any time an event of default, of which one potential outcome could be the accelerated repayment of the then outstanding loan balance under the facility. If we fail at any time to maintain a minimum required cash and short-term investments balance of at least $12.0 million, the bank has the option to require us to make a payment to reduce the outstanding balance under the credit facility to $6.0 million. If we fail at any time to maintain a minimum required cash and short-term investments balance of at least $10.0 million, the bank has the option to require us to make a payment to reduce the outstanding balance under the credit facility to $5.0 million. Finally, if we fail at any time to maintain a minimum required cash and short-term investments balance of at least $5.0 million we will be considered to be in default of the credit facility and the bank may take certain actions in relation to that default, including, but not limited to, requiring us to repay the entire outstanding balance under the credit facility.

As of December 31, 2005, we maintained a cash and cash equivalents balance of $37.7 million. During 2006, we anticipate average quarterly spending of approximately $8.0 million to $8.5 million to fund our operating activities, capital expenditures, and debt repayments, without giving effect to the impact of entering into any new collaborative agreements or disposing of our current headquarters and manufacturing facility. We believe that our existing cash and cash equivalents, expected revenue from collaborations and license arrangements, and interest income should be sufficient to meet our operating and capital requirements at least through 2006. Accordingly, we will need to raise substantial additional funds to avoid violating the debt covenant described above (See Overview in the Management s Discussion and Analysis of Financial Condition and Results of Operations section of this Form 10-K) and fund our operations until we are generating sufficient cash flow from operations.

The agreements comprising the credit facility also contain covenants that, among other things, require us to obtain consent from the bank prior to paying dividends, making certain investments, changing the nature of our business, assuming or guaranteeing the indebtedness of another entity or individual, selling or otherwise disposing of a substantial portion of our assets, or merging or consolidating with another entity.

A breach of any of the financial tests or other covenants in the agreements comprising the credit facility could result in a default under those agreements. Upon the occurrence of an event of default, the bank could elect to declare all amounts outstanding under the credit facility to be immediately due and payable, and terminate all commitments to

extend further credit.

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

We have incurred losses each year of our existence, including net losses of $51.8 million for the year ended December 31, 2005, $41.6 million for the year ended December 31, 2004, 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, 2005, we had an accumulated deficit of $239.2 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, and expand our business development and commercialization efforts. Our level of operating expenditures will vary depending upon the stage of development of our proprietary proteins and the number and nature of our collaborations. We may continue to incur substantial losses even if our revenues increase.

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

We have not yet 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 from corporate collaborations, license agreements, and investments. We do not know when or if we will complete any of our product development efforts, obtain regulatory approval for any product candidates incorporating our technologies, 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 these products gain market acceptance. The degree of market acceptance of these products will depend on a number of factors, including:

the timing of regulatory approvals in the countries, and for the uses, we seek;

the competitive environment;

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

the 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.

Risks Related to Development of Products and Technologies

We may be unable to develop next-generation therapeutic proteins.

We are seeking to use our enzymatic technologies to develop proprietary next-generation proteins, generally in collaboration with a partner. 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 producing or obtaining supplies of the protein on commercially reasonable terms, successfully modifying the protein using our enzymatic technologies, and achieving adequate yields of the next-generation protein. Even if a protein development program appears to be proceeding well in the early phases, a product candidate 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. If clinical trials are successful, it is possible that problems may arise later during commercialization. For example, we are aware that

certain marketed EPO products were associated with pure red cell aplasia that arose after marketing authorization. This highlights the fact that even after a product is approved for marketing, problems may arise that can negatively affect sales and increase costs.

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.

Preclinical and clinical trial results for our products may not be favorable.

In order to obtain regulatory approval for the commercial sale of any of our product candidates, we must conduct both preclinical studies and human clinical trials that demonstrate the product is safe and effective for the use for which we are seeking approval. Adverse results from studies, including clinical trials, could have a negative effect on our ability to obtain the approval of the FDA or other regulatory agencies.

We also may not be permitted to undertake or continue clinical trials for any of our product candidates in the future or may otherwise be unable to do so because acceptable candidates to participate in such trials are unavailable. Even if we are able to conduct such trials, we may not be able to demonstrate satisfactorily that the products are safe and effective and thus qualify for the regulatory approvals necessary to commercialize them.

Safety and efficacy results from preclinical studies involving animals and other models and from early clinical trials are often not accurate indicators of results of later-stage clinical trials that involve larger human populations, and, moreover, may not always be representative of results obtained while marketing an approved drug, particularly with regard to safety.

Proteins are uniquely susceptible to neutralizing antibodies that could result in diminished efficacy of our products.

Proteins that are foreign to a living body often provoke an immune response. Protein drugs produced by recombinant technology, even though they have the same primary amino acid sequence as a native human protein, sometimes provoke formation of antibodies that bind to the protein drug. Some such antibodies bind so as to prevent the protein drug from engaging its receptor, and thus neutralize the drug activity of the protein. Furthermore, neutralizing antibodies provoked by administration of a protein drug may react with endogenous proteins whose natural activity the drug was intended to supplement, thereby inducing a total lack of both therapeutic and natural activities in the patient. Such a condition can prove fatal. We will not know if the proteins we develop as product candidates will provoke neutralizing antibody responses in humans until they are evaluated in clinical trials. It is possible that our product candidates may be rendered ineffective for the therapeutic purpose for which they are intended or could induce harm to patients because of the neutralizing effect of antibodies to endogenous proteins in humans in response to our proteins.

Additionally, all protein drugs expressed by recombinant technology retain some trace of contaminating proteins from the host cells used to express the protein drug. These host cell proteins may increase the chances of an immunogenic response that could diminish the therapeutic efficacy of the protein. Our GlycoAdvance technology enables the use of protein drugs produced in insect cells, an expression system which has certain technical advantages in enabling the application of our technology to this protein, but for which no product to date has received marketing authorization in the U.S. or Europe. It is possible that our product candidates may be rendered ineffective for the therapeutic purpose for which they are intended because of the neutralizing effects of antibodies provoked by the presence of trace amounts of insect cell proteins in our drug preparations.

We have limited product development and commercial manufacturing experience, and face challenges unique to proteins.

To date, we have not manufactured, at commercial scale, any pharmaceutically active proteins nor the enzymes, sugar nucleotides or other reagents we use to modify proteins.

We and the third parties with whom we contract to manufacture our proteins face the significant, normal scale-up risks associated with protein manufacturing: proteins are difficult to produce; it is difficult to scale up protein manufacturing processes; and it is expensive to produce proteins. We also face special risks in connection

with our first product, NE-180, an EPO protein. Our success with this program will depend on our ability to have this protein manufactured, at commercial scale, in the insect cell expression system (the production source of NE-180), by a collaborator or supplier. We do not know if we will be able to locate a contract manufacturer outside of the U.S. that will be able to manufacture this protein at commercial scale and on economically feasible terms. To our knowledge, no therapeutic protein produced in this expression system has yet received marketing authorization in the U.S. or Europe, which means that we may face previously unidentified problems resulting from the use of this expression system and related regulatory challenges.

We will be relying on third parties to manufacture the proteins, enzymes, sugar nucleotides and other reagents we need to apply and commercialize our technologies. We may not be able to find parties willing and able to manufacture these compounds at acceptable prices, and we may become dependent on suppliers that could discontinue our supply arrangements or change supply terms to our disadvantage. Our success depends on our ability to have these compounds manufactured on a commercial scale or to obtain commercial quantities, in either case, at reasonable cost. We may not be able to procure sufficient quantities of the products we develop to meet our needs for preclinical or clinical development.

Any manufacturing facility and manufacturing process must adhere to the FDA s and/or other regulatory agencies evolving regulations on cGMP, which are enforced by the FDA and others through facilities inspection programs. The manufacture of products and key reagents 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, our contract manufacturers, or other suppliers may not meet these requirements.

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

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

We plan to rely to a large extent on collaborative partners to co-develop our products and to commercialize products made using our technologies. We currently have collaborative agreements with Novo Nordisk, BioGeneriX and MacroGenics. 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 or maintaining collaborative agreements for the co-development of our products or the commercialization of products incorporating our technologies;
- we may not be successful in applying 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 seek to develop other proprietary alternatives to our products or technologies;
- our collaborators may not commit sufficient resources to incorporating our technologies into their products;
- 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 may be terminated 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.

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.

Risks Related to Intellectual Property

Blocking patents or claims of infringement may stop or delay the development of our proprietary products.

Our commercial success depends in part on avoiding claims of infringement of the patents or proprietary rights of third parties. We have devoted significant resources to investigating the patent protection surrounding the proteins that are the subject of our development programs. The numerous patents, each with multiple claims, may be difficult to uncover and interpret, leading to uncertainty about our freedom to operate. It is possible that we will not be aware of issued patents or pending patent applications that are relevant to our product candidates because our searches do not find them, or pending patent applications because they are not yet publicly available. Our interpretation of patents could be challenged, leading to litigation, and we could face claims of infringement of rights of which we are unaware.

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 by others and these patents could delay our ability to market a long-acting EPO in the U.S. As we proceed with this program and 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.

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. In particular, one company that produces products that will likely be in direct competition with our current product candidates has aggressively defended the patents related to its products and this could increase the likelihood of litigation or 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.

Third parties from time to time may assert that we are infringing their patents, trade secrets or know-how, although we believe our product candidates do not infringe the products, trade secrets or know-how of third parties. In addition, patents may issue in the future 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 or be unable to proceed. 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.

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. We are seeking to develop patent protection for therapeutic proteins that

include numerous claims for composition of matter, methods of use, and methods of making. Legal standards relating to the validity and scope of claims in our technology field are still evolving. Therefore, the degree of future protection in the U.S. and other countries 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.

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 costs 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. Furthermore, patent protection available to us may vary in different jurisdictions. In particular, the laws in some countries provide little patent protection.

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.

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.

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. The ownership of patents exclusively licensed to us may be subject to challenge if inventorship was not adequately investigated and represented. 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.

Risks Related to Competition

Our competitors may develop better or more successful products.

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 that 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, Nektar Therapeutics, BioRexis, Human Genome Sciences 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, Roche, Shire, Maxygen, Fibrogen, Affymax and Syntonix. Other companies are active in this area, and we expect that competition will increase. We are also aware that there are several companies engaged in glycobiology research.

In addition, we may compete with companies commercializing first-generation protein therapeutics, as a result of pricing practices or reimbursement limitations. Even if we succeed in developing and marketing products that have significant advantages over first-generation products, if first-generation products are available at a lower out-of-pocket cost to the consumer, health-care providers and consumers may choose first-generation products instead of next-generation versions.

Compared to us, many of our likely and potential competitors 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 or 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 enzymatically modifying 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 proven abbreviated regulatory pathway for follow-on biologics, this possibility is under discussion in the U.S. and other jurisdictions and has been adopted in part in Europe. 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. The advancement of our business is dependent upon our management team s ability to evaluate collaboration opportunities and on their ability to focus our 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 our business. The loss of the services of existing personnel, as well as the failure to recruit additional key scientific, technical and managerial personnel in a timely manner, could harm our research and development programs and our ability to manage day-to-day operations, attract collaboration partners, attract and retain other employees, and generate revenues. We do not maintain key person 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 or may encounter long delays and large expenditures in obtaining such 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 Europe and in 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.

In addition, the U.S. or other regulatory agencies could, at any time in the regulatory approval process, place the regulatory submission for a product candidate on hold pending the receipt, review and approval of additional information. The IND for our first product candidate, NE-180, is currently on hold in the U.S. There is the risk that we will not be taken off hold and will therefore be unable to proceed with clinical trials of NE-180 in the U.S.

We and our collaborators intend to base our submissions for regulatory approval and the information contained in such submissions on our understanding of the requirements of the FDA and its foreign counterparts. If additional information is required, we may face delays and additional costs.

The specific risks of protein drugs may result in the application of more stringent regulatory requirements prior to approval of our product candidates. We face special challenges in connection with the development of proteins produced in the insect cell expression system. To our knowledge, no therapeutic protein for human use produced in this expression system has been submitted for marketing authorization in the U.S. or Europe, and we may encounter long delays and large expenditures or other regulatory hurdles in connection with the approval process for a product produced in this expression system.

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, and we will have already spent significant sums in pursuing approval.

We anticipate that the development of our next-generation proprietary proteins will involve a traditional development program, including clinical trials. Any new governmental regulations may delay or alter regulatory approval of any product candidate manufactured using our technology. 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 cannot predict the impact of adverse governmental action that might arise from future legislative and administrative action.

Even if we or our collaborators are successful in obtaining regulatory approvals for any of our products, our or their manufacturing processes will 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 or our collaborators have not complied with regulations in the research and development of a product candidate or the manufacture and control of our reagents, then we or our collaborators may not obtain necessary approvals to market and sell the product candidate.

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 and our collaborators 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. 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. It is possible that reimbursement may be limited to that which is available for first-generation versions of one or more of our or our collaborator s products, making it harder for us and our collaborators to realize an appropriate return.

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 corrosive, toxic and flammable chemicals, 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 or our collaborators 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.

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.

Risk 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, since March 1, 2005, the price of our common stock reached a high of $4.49 per share in July 2005 and a low of $1.70 per share in November 2005.

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 for our common stock, including:

preclinical and clinical trial results;

product development delays;

regulatory 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;

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 RISK FACTORS occurred, of 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 Risk

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

We have entered into some agreements denominated, wholly or partly, in Euros or other foreign currencies, and, in the future, we may enter into additional, significant agreements denominated in foreign currencies. If the values of these currencies increase against the dollar, our costs would increase. 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 1B. UNRESOLVED STAFF COMMENTS.

None.

ITEM 2. PROPERTIES.

We own, subject to our mortgages, approximately 50,000 square feet of manufacturing, laboratory, and corporate office space (Witmer Road facility) in Horsham, Pennsylvania. In November 2005, we commenced efforts to dispose of the Witmer Road facility in connection with the restructuring of operations we announced in August 2005.

In July 2002, we entered into a 20-year lease of a nearby building of approximately 40,000 square feet, of which approximately 25,000 square feet were converted into laboratory and office space during the first half of 2004, leaving approximately 15,000 square feet available for future expansion. We also lease approximately 5,000 square feet of warehouse space in another nearby building in Horsham. In addition, we lease approximately 10,000 square feet of laboratory and office space in San Diego, California. As of October 31, 2005, we ceased operations at our San Diego facility. The initial term of the San Diego lease ends in March 2006, at which time we intend to terminate the lease.

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 2005.

PART II

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

Our common stock is listed on The NASDAQ National Market under the symbol NTEC. We commenced trading on The NASDAQ National 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, 2004		
First Quarter	$ 13.80	$ 8.73
Second Quarter	10.62	6.50
Third Quarter	8.78	6.45
Fourth Quarter	8.19	6.10
Year Ended December 31, 2005		
First Quarter	7.25	2.49
Second Quarter	3.23	1.95
Third Quarter	4.49	2.15
Fourth Quarter	2.85	1.70
Year Ended December 31, 2006		
First Quarter (through March 3, 2006)	3.95	1.85

As of March 3, 2006, there were approximately 200 record holders and 4,400 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. Moreover, under the terms of our credit agreement with our bank, we are not permitted to pay any dividends without its written consent.

ITEM 6. SELECTED FINANCIAL DATA.

The following Statements of Operations and Balance Sheet Data for each of the years in the five-year period ended December 31, 2005 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,				
	2005	2004	2003	2002	2001
	(in thousands, except per share data)				
Statements of Operations Data:					
Revenue from collaborative agreements	$ 6,137	$ 5,070	$ 1,435	$ 4,813	$ 1,266
Operating expenses:					
Research and development	33,136	34,672	26,821	21,481	14,857
General and administrative	10,878	11,711	11,148	12,510	9,374
Restructuring charges	14,206				
Total operating expenses	58,220	46,383	37,969	33,991	24,231
Operating loss	(52,083)	(41,313)	(36,534)	(29,178)	(22,965)
Other income	22			1,653	6,120
Impairment of equity securities			(1,250)		
Interest income (expense), net	222	(329)	103	1,108	3,516
Net loss	$ (51,839)	$ (41,642)	$ (37,681)	$ (26,417)	$ (13,329)
Basic and diluted net loss per share	$ (1.64)	$ (1.82)	$ (2.14)	$ (1.85)	$ (0.95)
Weighted-average shares outstanding used in computing basic and diluted net loss per share	31,590	22,898	17,611	14,259	14,032
Balance Sheet Data:					
Cash, cash equivalents and marketable securities	$ 37,738	$ 45,048	$ 53,060	$ 41,040	$ 76,245

Total assets	65,363	90,731	94,845	83,092	105,786
Total debt and capital lease obligations	14,454	18,345	10,601	7,411	6,200
Accumulated deficit	(239,220)	(187,381)	(145,739)	(108,058)	(81,641)
Total stockholders equity	40,117	60,854	72,213	70,685	93,946

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

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 that typically may be identified by use of terms such as anticipate, believe, estimate, plan, may, expect, intend, could, potential, and similar expressions, alth forward-looking statements are expressed differently. These forward-looking statements include, among others, the statements about our:

- estimate that our existing cash and cash equivalents, expected revenue from collaborations and license agreements, and interest income should be sufficient to meet our operating and capital requirements at least through 2006;
- expected losses;
- expectations for future capital requirements;
- expectations for increases in operating expenses;
- expectations for increases in research and development, and marketing, general and administrative expenses in order to develop products, procure commercial quantities of reagents and products, and commercialize our technology;
- expectations regarding the scope and expiration of patents;
- expectations regarding the timing of preclinical activities, regulatory meetings and submissions, as well as the progression of clinical trials, for NE-180 and preclinical activities and the initiation of clinical trials for GlycoPEG-GCSF;
- expectations for the development of long-acting versions of EPO and G-CSF, and subsequent proprietary drug candidates;
- expectations as to the costs and benefits of our plans to dispose of our Witmer Road facility;
- expectations regarding net cash utilization;
- expectations for generating revenue; and
- expectations regarding the timing and character of new or expanded collaborations and for the performance of our existing collaboration partners in connection with the development and commercialization of products incorporating our technologies.

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. Potential risks and uncertainties that could affect our actual results include the following:

- our ability to obtain the funds necessary for our operations;
- our ability to meet forecasted timelines due to internal or external causes;
- our ability to satisfy the FDA s request for additional information and to obtain clearance from the FDA to commence a Phase I clinical trial for NE-180 in the U.S.;

our preclinical and clinical results for our products may not be favorable;

our ability to develop commercial-scale manufacturing processes for our products and reagents, either independently or in collaboration with others;

our ability to enter into and maintain collaborative arrangements;

our ability to obtain adequate sources of proteins and reagents either manufactured internally or sourced externally;

our ability to develop and commercialize products without infringing the patent or intellectual property rights of others;

our ability to expand and protect our intellectual property and to operate without infringing the rights of others;

our ability and our collaborators ability to develop and commercialize therapeutic proteins and our ability to commercialize our technologies;

our ability to attract and retain key personnel;

our ability to compete successfully in an intensely competitive field;

our ability to renovate our facilities as required for our operations; and

general economic conditions.

These and other risks and uncertainties that could affect our actual results are discussed in this report, particularly in Item 1A of Part I of this Form 10-K in the section entitled Risk Factors.

Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee future results, events, levels of activity, performance, or achievements. We do not assume responsibility for the accuracy and completeness of the forward-looking statements other than as required by applicable law. We do not undertake any duty to update any of the forward-looking statements after the date of this report to conform them to actual results, except as required by the federal securities laws.

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 using our enzymatic technologies to develop proprietary drugs, focusing primarily on therapeutic proteins. We believe that our core enzymatic technologies, GlycoAdvance and GlycoPEGylation, improve the drug properties of therapeutic proteins by building out, and attaching polyethylene glycol (PEG) to, carbohydrate structures on the proteins. We are using our technologies to develop proprietary versions of protein drugs with proven safety and efficacy and to improve the therapeutic profiles of proteins being developed by our partners. We expect these modified proteins to offer significant advantages, including less frequent dosing and possibly improved efficacy, over the original versions of the drugs now on the market, as well as to meet or exceed the pharmacokinetic profile of next-generation versions of the drugs now on the market. We believe this strategy of targeting drugs with proven safety and efficacy allows us to lower the risk profile of our proprietary development portfolio as compared to *de novo* protein drug development.

We have incurred operating losses each year since our inception. As of December 31, 2005, we had an accumulated deficit of $239,220,000. We expect additional losses in 2006 and over the next several years as we continue product research and development efforts and expand our intellectual property portfolio. 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 and cash equivalents, expected revenue from collaborations and license arrangements, and interest income should be sufficient to meet our operating and capital requirements at least through 2006, although changes in our collaborative relationships or our business, whether or not initiated by us, may cause us to deplete our cash and cash equivalents sooner than the above estimate. Under agreements we entered into with a bank during the first quarter of 2004, we have agreed to limit our total outstanding debt to $22,000,000. As of December 31, 2005, our total outstanding debt was $14,454,000. In March 2006, we entered into amendments of our agreements with the bank. These amendments, effective March 1, 2006, revised the minimum liquidity requirements, increased the interest rate applicable to the outstanding balance and added a prepayment premium to be paid in the event we repay the loan earlier than as set forth in the agreements. Pursuant to the amendments, if we fail at any time to maintain a minimum required cash and short-term investments balance of at least $12.0 million, the bank has the option to require us to make a payment to reduce the outstanding balance under the credit facility to $6.0 million. If we fail at any time to maintain a minimum required cash and short-term investments balance of at least $10.0 million, the bank has the option to require us to make a payment to reduce the outstanding balance under the credit facility to $5.0 million. Finally, if we fail at any time to maintain a minimum required cash and short-term investments balance of at least $5.0 million we will be considered to be in default of the credit facility and the bank may take certain actions in relation to that default, including, but not limited to, requiring us to repay the entire outstanding balance under the credit facility. See Financing Activities Debt Financing Activities Term Loan from Bank and Industrial Development Authority Bond 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 $37,738,000 in cash and cash equivalents as of December 31, 2005, compared to $45,048,000 in cash and cash equivalents as of December 31, 2004. The decrease for 2005 was primarily attributable to the use of cash to fund our operating activities, capital expenditures, and debt repayments, which were partly offset by proceeds of equity and debt financings. During 2006, we anticipate our average quarterly spending of approximately $8.0 million to $8.5 million to fund our operating activities, capital expenditures, and debt repayments, without giving effect to the impact of entering into any new collaborative agreements or disposing of our current headquarters and manufacturing facility. We believe that our existing cash and cash equivalents, expected revenue from collaborations and license arrangements, and interest income should be sufficient to meet our operating and capital requirements at least through 2006. Accordingly, we will need to raise substantial additional funds to avoid violating the debt covenant described above and to fund our operations until we are generating sufficient cash flow from operations. If we are unable to raise additional capital when required, we may need to delay, scale back, or eliminate some of our research and development programs.

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. 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. Because our 2006 revenues could be substantially affected by entering into new collaborations and on the financial terms of any new collaborations, we cannot estimate our 2006 revenues. Other than revenues from our collaborations with Novo Nordisk and BioGeneriX, and any future collaborations with others, we do not expect to generate significant revenues until such time as products using our technologies are commercialized, which is not expected during the next 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 until we are generating sufficient cash flow from operations.

2005 Restructuring

In August 2005, we implemented a restructuring of operations to enable an enhanced focus on next-generation proteins, to allow for the anticipated transfer of production of proteins and reagents to our collaborative partners and contract manufacturers now that our programs are more mature, and to reduce cash burn. Our future requirements for internally manufactured products will be substantially lower than the capacity of our 24,000 square-foot pilot manufacturing facility. Therefore, we commenced efforts to dispose of our current headquarters and pilot manufacturing facility (Witmer Road facility), which we own subject to mortgages supporting our term loan and industrial development authority bond (both are more fully described in the Liquidity and Capital Resources section of this Form 10-K under the heading Financing Activities Debt Financing Activities Term Loan from Bank and Industrial Development Authority Bond). Upon completion of the restructuring, we had reduced the size of our workforce by approximately 25% since the end of the first quarter of 2005. Our net loss for 2005 included $14,206,000 of charges related to this restructuring, including $13,187,000 of non-cash property and equipment impairment charges and $1,019,000 of payments for employee severance and facility closure costs. We expect to realize annualized savings from the restructuring of between $6,000,000 and $8,000,000.

Property and Equipment Impairment Charges

As a result of our decision to dispose of the Witmer Road facility, we concluded that identifiable cash flows could be assigned to the Witmer Road facility and related equipment. To determine the appropriate carrying value of these assets, we used a probability-weighted approach of estimated cash flows to be received upon a range of possible disposition outcomes. We based our estimates of potential cash flows related to possible disposition outcomes on conversations with commercial real estate firms that have both knowledge of recent history of sales and expertise in marketing and selling similar facilities. Based on those estimates, we recorded a non-cash impairment charge of $13,000,000, which was included in restructuring charges on our statements of operations, on our Witmer Road facility and related equipment. Also as part of the restructuring, we centralized research activities in Horsham, Pennsylvania by ending operations in our leased facility in San Diego, California. We recorded a non-cash impairment charge of $187,000, which was also included in restructuring charges on our statements of operations, related to property and equipment located in the San Diego facility.

Employee Severance and Facility Closure Costs

During 2005, we recorded $867,000, which was also included in restructuring charges on our statements of operations, of employee severance costs related to the restructuring. We also recorded a facility closure charge of $152,000 in restructuring charges on our statements of operations for the operating lease related to the San Diego facility. This charge was based on an estimate of the present value of the loss we would incur over the remaining term of the lease. Because the remaining lease term extended for only five months beyond our cease-use date of the facility, we assumed no sublease income in our calculation.

Operating Activities

During 2005, our operating activities consumed cash of $33,069,000, compared to $36,744,000 in 2004. The decrease of $3,675,000 in net cash consumed for 2005 operating activities is substantially the result of $637,000 of cash provided during 2005 compared to $1,470,000 of cash used during 2004 to fund changes in operating assets and liabilities, primarily due to a decrease of $1,809,000 in accounts receivable during 2005. Also contributing to a decrease in net cash consumed by operating activities was an increase in net interest income of $551,000 during 2005 compared to 2004. Fluctuations in operating items vary period-to-period due to, among other factors, the timing of research and development activities, such as the preparation and initiation of preclinical trials.

Investing Activities

During 2005 and 2004, cash expenditures for property, plant, and equipment were $792,000 and $9,844,000, respectively. The facility improvement project described below contributed significantly to our capital expenditures during 2004.

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 on approximately 25,000 square feet of the facility, leaving approximately 15,000 square feet available for future expansion. In April 2004, we occupied the facility and began amortizing the cost of $10,175,000 of the improvements. During 2004, we entered into agreements with a bank for the purpose of funding these improvements. See Financing Activities Debt Financing Activities Term Loan from Bank and Industrial Development Authority Bond below for a description of the material features of this borrowing.

In 2006, we expect our investment in capital expenditures to be approximately $1,000,000 to $1,500,000, excluding the cost of any leasehold improvements we need in order to accomplish a consolidation of our research, development and administrative operations upon the disposition of our current headquarters and pilot manufacturing facility (Witmer Road facility). See 2005 Restructuring above for a discussion of our efforts to dispose of the Witmer Road facility. We may finance some or all of these capital expenditures through capital leases or the issuance of new debt or equity. We may finance capital expenditures through the issuance of new debt, to the extent that we are allowed to do so under our existing bank covenants. The terms of new debt could require us 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.

Financing Activities

Equity Financing Activities

In February 2005, we offered and sold 8,050,000 shares of our common stock at a public offering price of $4.00 per share, generating net proceeds of $30,006,000. In May 2004, we sold 4,733,476 shares of common stock in a registered direct offering to a number of institutional and individual investors, including 812,408 shares sold to officers and an investment fund affiliated with a director, at a price of $6.77 per share, generating net proceeds of $29,928,000.

Debt Financing Activities

Our total debt decreased by $3,891,000 to $14,454,000 at December 31, 2005, compared to $18,345,000 at December 31, 2004. This decrease primarily resulted from $5,365,000 of debt principal repayments during 2005. Partially offsetting the debt repayments were $1,484,000 in proceeds from the issuance of debt during 2005.

Note Payable Secured by Insurance Policies

In March 2005, we borrowed $701,000 to finance the insurance policy premiums due on certain insurance policies. We made the last payment in December 2005 and, therefore, there was no outstanding principal balance under this agreement as of December 31, 2005. The interest was calculated based on an annual percentage rate of 3.91%. To secure payment of the amounts financed, we granted the lender a security interest in all of our right, title and interest to the insurance policies.

Term Loan from Bank and Industrial Development Authority Bond

During the first quarter of 2004, we and a bank entered into agreements under which the bank acquired and reissued the $1,000,000 outstanding of our tax-exempt Industrial Development Authority bond. In addition, we borrowed $8,000,000 from the bank, of which $6,200,000 funded improvements to our leased facility, which we occupied in April 2004, in Horsham, PA. As of December 31, 2005, we owed the bank $8,111,000. As discussed in 2005 Restructuring above, we have commenced efforts to dispose of our current headquarters and pilot manufacturing facility (Witmer Road facility). If we dispose of the Witmer Road facility, we will be required to repay the outstanding balance to the bank, whether or not the proceeds from the disposition of the facility exceed the outstanding loan balance.

During 2006, we will be required to make principal payments totaling $889,000 under these agreements. The interest rate on the bond and bank debt varies quarterly, depending on 90-day LIBOR rates. At December 31,

2005, the 90-day LIBOR was 4.54%. We have the option each quarter to incur interest on the outstanding principal at the LIBOR-based variable interest rate or a fixed rate offered by our bank.

For the $8,000,000 term loan, interest accrues at an interest rate equal to the 90-day LIBOR plus 3.0%. During 2005, the weighted-average annual interest rate for the term loan was 6.5%. We made quarterly, interest-only payments prior to March 31, 2005. Commencing on March 31, 2005, we began to make quarterly principal payments of $222,000 plus interest. We are required to make these payments over the remaining term of the ten-year loan period. Pursuant to the amendments to our agreements with the bank discussed below, after March 1, 2006, interest on the term loan began to accrue at an interest rate equal to the 90-day LIBOR plus 5.0%.

For the $1,000,000 Industrial Development Authority bond, we are making quarterly, interest-only payments for ten years at an interest rate equal to the 90-day LIBOR plus 1.5%, followed by a single repayment of principal at the end of the ten-year loan period. If the 90-day LIBOR at the beginning of any calendar quarter is between 4.0% and 6.0%, the bond will bear interest at the 90-day LIBOR plus 1.25%. If the 90-day LIBOR at the beginning of any calendar quarter exceeds 6.0%, the bond will bear interest at the 90-day LIBOR plus 1.0%. During 2005, the weighted-average annual interest rate for the bond was 4.8%. Pursuant to the amendments to our agreements with the bank discussed below, after March 1, 2006, interest on the Industrial Development Authority bond began to accrue at an interest rate equal to the 90-day LIBOR plus 3.5%.

To provide security for these borrowings, we granted a first mortgage to our bank on the land and building where our present headquarters are located, as well as a security interest of first priority on certain improvements, certain equipment, and other tangible personal property. Under our agreements with the bank, if the bank determines a material adverse change has occurred in our business, financial condition, results of operations, or business prospects, the bank in its sole discretion may declare at any time an event of default, of which one potential outcome could be the accelerated repayment of the loan balance, which was $8,111,000 as of December 31, 2005. Under our agreements with the bank, we agreed to limit our total outstanding debt to $22,000,000. As of December 31, 2005, our total outstanding debt was $14,454,000. Prior to the execution of the amendments discussed below, at any time after January 30, 2008, or if we failed to maintain a minimum required cash and short-term investments balance of at least $22,000,000, our bank would have had the option to require additional collateral from us in the form of a security interest in certain cash and short-term investments, or in the form of a letter of credit. The agreements with our bank also contain covenants that, among other things, require us to obtain consent from the bank prior to paying dividends, making certain investments, changing the nature of our business, assuming or guaranteeing the indebtedness of another entity or individual, selling or otherwise disposing of a substantial portion of our assets, and merging or consolidating with another entity.

In March 2006, we entered into amendments of our agreements with the bank. These amendments, effective March 1, 2006, revised the minimum liquidity requirements, increased the interest rate applicable to the outstanding balance and added a prepayment premium to be paid in the event we repay the loan earlier than as set forth in the agreements. Pursuant to the amendments, if we fail at any time to maintain a minimum required cash and short-term investments balance of at least $12.0 million, the bank has the option to require us to make a payment to reduce the outstanding balance under the credit facility to $6.0 million. If we fail at any time to maintain a minimum required cash and short-term investments balance of at least $10.0 million, the bank has the option to require us to make a payment to reduce the outstanding balance under the credit facility to $5.0 million. Finally, if we fail at any time to maintain a minimum required cash and short-term investments balance of at least $5.0 million we will be considered to be in default of the credit facility and the bank may take certain actions in relation to that default, including, but not limited to, requiring us to repay the entire outstanding balance under the credit facility.

Term Loan from Landlord

In May 2004, we borrowed $1,500,000 from the landlord of our leased facilities in Horsham, Pennsylvania. The terms of the financing require us to pay monthly principal and interest payments over 48 months at an interest rate of 13%. As of December 31, 2005, we owed the landlord $997,000. During 2006, we expect to make principal and interest payments totaling $483,000 under this agreement.

Equipment Loans

We borrowed $783,000, $3,612,000, and $4,986,000 during 2005, 2004, and 2003, respectively, from an equipment lender to finance the purchase of equipment and facility improvements, which collateralize the amounts borrowed. The terms of the financings require us to make monthly principal and interest payments through January 2009 at interest rates ranging from 8.00% to 9.44%. As of December 31, 2005, we owed the equipment lender $5,075,000. During 2006, we will be required to make principal and interest payments totaling $2,939,000 under these agreements. As discussed in 2005 Restructuring above, we have commenced efforts to dispose of our current headquarters and pilot manufacturing facility (Witmer Road facility). If we dispose of the Witmer Road facility, we will be required to repay some of the outstanding balance to the equipment lender.

Capital Lease Obligations

We did not enter into any agreements with capital lease obligations during 2005. We entered into agreements with capital lease obligations during 2004 and 2003 for equipment with a value of $184,000 and $787,000, respectively. The terms of existing leases require us to make monthly payments through August 2009. As of December 31, 2005, the present value of aggregate minimum lease payments under these agreements was $271,000. Under these agreements, we will be required to make principal and interest payments totaling $179,000 during 2006.

Operating Leases

We lease laboratory, office, warehouse facilities, and equipment under operating lease agreements. In April 2001, we entered into a lease agreement for approximately 10,000 square feet of laboratory and office space in San Diego, California. As part of the restructuring announced in August 2005 and described in the Liquidity and Capital Resources section of this Form 10-K, we centralized research activities in Horsham, Pennsylvania by ending operations in our leased facility in San Diego, California. As of October 31, 2005, we ceased operations at our San Diego facility. The initial term of the San Diego lease ends on March 31, 2006, at which time we intend to terminate the lease.

We lease approximately 5,000 square feet of office and warehouse space in Horsham, Pennsylvania under a lease agreement that expires April 2007. In February 2002, we entered into a lease agreement for approximately 40,000 square feet of laboratory and office space in another nearby building in Horsham, 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 laboratory, office, and warehouse facility leases contain escalation clauses, under which the base rent increases annually by 2%. Our rental expense for the years ended December 31, 2005, 2004, and 2003 was $951,000, $981,000, and $923,000, respectively.

Summary of Contractual Obligations

The following table summarizes our obligations to make future payments under current contracts as of December 31, 2005:

		Payments due by period			
	Total	Less than 1 Year	1 - 3 Years	4 - 5 Years	After 5 Years
Long-term debt obligations[1]					
Debt maturities	$14,183,000	$3,868,000	$4,766,000	$1,882,000	$ 3,667,000
Contractual interest	5,012,000	980,000	1,327,000	1,079,000	1,626,000
Capital lease obligations[2]					
Debt maturities	271,000	163,000	101,000	7,000	¾
Contractual interest	27,000	16,000	11,000	¾	¾
Operating leases[3]	8,818,000	708,000	962,000	936,000	6,212,000
Purchase obligations[4]	1,022,000	982,000	40,000	¾	¾
Other liabilities reflected on our balance sheet under GAAP[5]	351,000	351,000	¾	¾	¾
Total contractual obligations	$29,684,000	$7,068,000	$7,207,000	$3,904,000	$11,505,000

1. See Financing Activities Debt Financing Activities in this Liquidity and Capital Resources section and Note 7 of the Notes to Financial Statements included in Item 8 of this Form 10-K for a description of the material features of our long-term debt. Contractual interest is the interest we contracted to pay on the long-term debt obligations. We had $8,111,000 of long-term debt subject to variable interest rates at December 31, 2005. The rate assumed for the variable interest component of the contractual interest obligation was the applicable rate in effect at December 31, 2005.

2. See Financing Activities Capital Lease Obligations in this Liquidity and Capital Resources section and Note 14 of the Notes to Financial Statements included in Item 8 of this Form 10-K for a description of the material features of our capital lease obligations. At December 31, 2005, the present value of our capital lease obligations was $271,000 and the amount of imputed interest, calculated using an assumed incremental borrowing rate at the time we entered into the capital lease obligations, was $27,000.

3. See Note 14 of the Notes to Financial Statements included in Item 8 of this Form 10-K for a description of our significant operating leases.

4. Includes our commitments as of December 31, 2005 to purchase goods and services from various suppliers.

5. Represents the remaining payments as of December 31, 2005 under separation and retirement agreements with former officers of the Company. These agreements are described in Note 14 of the Notes to Financial Statements included in Item 8 of 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 current or future effect on our financial condition, changes in financial condition, revenues or expenses, results of operations, liquidity, capital expenditures, or capital resources.

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 U.S. generally accepted accounting principles. 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.

Accounting for Restructuring Costs

To account for exit or disposal activities, such as the restructuring described in Overview in the Liquidity and Capital Resources section of this Form 10-K, we apply Statement of Financial Accounting Standards (SFAS) No. 146, *Accounting for Costs Associated with Exit or Disposal Activities* (SFAS No. 146), which requires a liability for a cost associated with an exit or disposal activity to be recognized and measured initially at fair value only when the liability is incurred. It does not apply to costs associated with a disposal activity covered by SFAS No. 144, *Accounting for the Impairment or Disposal of Long-Lived Assets* (SFAS No. 144). The restructuring charges recorded by us during the six months ended December 31, 2005 were comprised primarily of costs to reduce property and equipment to fair value and to reduce our workforce. Our net loss for the year ended December 31, 2005 included $14,206,000 of charges related to this restructuring, including $13,187,000 of non-cash property and equipment impairment charges and $1,019,000 of payments for employee severance and facility closure costs.

Under SFAS No. 144, any impairment of property and equipment to be recognized is measured by the amount by which the carrying amount of the assets exceeds the fair value of the assets. To determine the fair value of assets that are not likely to be used over their remaining useful economic life, we use a probability-weighted approach of estimated cash flows to be received upon a range of possible disposition outcomes. In August 2005, we announced we would evaluate alternatives for our current headquarters and pilot manufacturing facility (Witmer Road facility), which we own subject to a mortgage, including the potential disposition of the facility and further consolidation of our research, development and administrative operations into a currently leased facility that is also located in Horsham, Pennsylvania. Following the announcement, we concluded that identifiable cash flows could be assigned to the Witmer Road facility and related equipment. We based our estimates of potential cash flows related to possible disposition outcomes on conversations with commercial real estate firms that have both knowledge of recent history of sales and expertise in marketing and selling similar facilities. These estimates may turn out to be incorrect and our actual cash flows may be materially different from our estimates.

Our estimates of future liabilities may change, requiring us to record additional restructuring charges or reduce the amount of liabilities recorded. At the end of each reporting period, we evaluate the remaining accrued balances to ensure their adequacy, that no excess accruals are retained and the utilization of the provisions are for their intended purposes in accordance with developed exit plans. We periodically evaluate current available information and adjust our restructuring reserve as necessary.

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 2003. Upfront fees and payments received from non-substantive milestones, such as the passage of time, 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 received 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 substantive 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.

Stock-based Employee Compensation

We apply Accounting Principles Board Opinion No. 25, *Accounting for Stock Issued to Employees*, 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 SFAS No. 123, *Accounting for Stock-Based Compensation*, as amended by SFAS No. 148, *Accounting for Stock-Based Compensation Transition and Disclosure.* The stock-based employee compensation expense determined under the fair value-based method was calculated as of the date of grant of individual awards using the Black-Scholes option-pricing model. The volatility and expected term assumptions have the most significant effect on the results obtained from the Black-Scholes option-pricing model. The volatility assumption for each year has been estimated with reference to our historical volatility. The expected term assumption for each award has been estimated with reference to prior option exercise history, as well as the simplified method outlined by the SEC in Staff Accounting Bulletin No. 107, *Share-based Payment*. The following table contains the assumptions used in the Black-Scholes option-pricing model in each year to value stock-based compensation:

	Year ended December 31,		
	2005	2004	2003
Expected life (years):			
Stock options	6.7	6.6	5.5
Employee stock purchase plan	N/A	1.3	1.8
Risk-free interest rate:			
Stock options	4.1%	3.5%	3.0%
Employee stock purchase plan	N/A	1.6%	2.9%
Volatility	75%	80%	80%
Dividend yield	0%	0%	0%

Impairment of Long-Lived Assets

We evaluate our long-lived assets for impairment at least annually and whenever indicators of impairment exist, such as our August 2005 restructuring described in Overview in the Liquidity and Capital Resources section of this Form 10-K. Because our history of negative operating cash flows is an indicator of impairment, we annually compare the market value of our equity and debt to the carrying value of our net assets. The market value of our equity and debt exceeded the carrying value of our net assets as of December 31, 2005 and, therefore, we did not record any impairment of long-lived assets beyond the impairment recorded in connection with our August 2005 restructuring.

Estimating Expenses from Contract Research and Development Service Providers

Some of our research and development is conducted by third parties, including contract research and development service providers. At the end of each quarter, we compare the payments made to each service provider to the estimated progress toward completion of the research or development objectives. Such estimates are subject to change as additional information becomes available. Depending on the timing of payments to the service providers and the estimated service provided, we record prepaid or accrued expense relating to these costs. We monitor each of these factors to the extent possible and adjust estimates accordingly.

Results of Operations

Years Ended December 31, 2005 and 2004 and Outlook for 2006

Our net loss for the year ended December 31, 2005 was $51,839,000 compared to $41,642,000 for the corresponding period in 2004. The following section explains the trends within each component of net loss for 2005 compared to 2004 and provides our estimate of trends for 2006 for each component.

Revenue from Collaborative Agreements. 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.

Revenue from collaborative agreements increased to $6,137,000 in 2005 from $5,070,000 in 2004 due to research and development funding under our collaborations with Novo Nordisk and BioGeneriX.

During the years ended December 31, 2005, 2004, and 2003, one customer accounted for 46%, 66%, and 48%, respectively, of total revenues. Another customer accounted for 54% and 34% of our total revenues during the years ended December 31, 2005 and 2004 respectively.

Because our 2006 revenues could be substantially affected by entering into new collaborations and on the financial terms of any new collaborations, we cannot estimate our 2006 revenues. 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, if ever, 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 levels of effort committed and made by our collaborative partners. Even if we achieve technical success in developing drug candidates, our collaborative partners may discontinue development, may not devote the resources necessary to complete development and commence marketing of these products, or they may not successfully market potential products.

Research and Development Expense . Our proprietary drug development portfolio consists of two therapeutic protein candidates: GlycoPEG-EPO (NE-180) and GlycoPEG-GCSF. Erythropoietin (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 chemotherapy-induced anemia and anemia associated with chronic renal failure. Based on early preclinical studies, we believe it is feasible to develop a long-acting EPO through GlycoPEGylation. In February 2006, we initiated a Phase I clinical trial for NE-180 in a Western European country. We expect this clinical trial to conclude by mid-2006. In the U.S., our Investigational New Drug application (IND) for NE-180 is currently on clinical hold with the U.S. Food and Drug Administration (FDA). We anticipate finalizing our Complete Response to the FDA in early 2006. The timing of submission of this response to the FDA will depend upon the evolution of our regulatory and clinical strategy. The early clinical development of NE-180 could be carried out entirely in Europe.

Granulocyte colony stimulating factor (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 myelosuppressive chemotherapy. Based on our proof-of-concept data and preclinical development activities, we believe it is feasible to develop a long-acting G-CSF through GlycoPEGylation. We expect that by the end of the first quarter of 2006, in collaboration with our partner, BioGeneriX, we will commence the regulatory process in a European country.

We conduct exploratory research, both independently and with collaborators, on therapeutic candidates, primarily proteins, for development using our enzymatic technologies. Successful candidates may be advanced for development through our own proprietary drug program or through our partnering and licensing program, or a combination of the two. Although our primary focus is the development of long-acting proteins, we are also conducting research to assess opportunities to use our enzymatic technologies in other areas, such as glycopeptides and glycolipids. We expect to continue this research during 2006.

Our current research and development projects are divided between two categories: (i) GlycoAdvance and GlycoPEGylation and (ii) Other Glycotechnology Programs, which includes projects investigating opportunities to use our enzymatic technologies in other areas, such as glycolipids. 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	Clinical (Phase I)	Active
Improved granulocyte colony stimulating factor	Preclinical	Active
Other protein projects	Research	Active
Other Glycotechnology Programs:		
Non-protein therapeutic applications	Research	Active
Nutritional applications	N/A	Evaluating outlicensing opportunities

The process of bringing drugs from the preclinical research and development stage through Phase I, Phase II, and Phase III clinical trials to FDA or other regulatory approval is time consuming and expensive. Because our announced product candidates are currently in the early clinical and preclinical stages, and there are a variety of potential intermediate clinical and non-clinical outcomes that are inherent in drug development, we cannot reasonably estimate either the timing or 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.

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 decreased to $33,136,000 in 2005 from $34,672,000 in 2004. During 2006, excluding the effect of the adoption of SFAS No. 123 (Revised 2004), *Share-Based Payment* (SFAS No. 123R), we expect our research and development expenses to be lower than they were in 2005 as a result of the restructuring we implemented in August 2005. The following table illustrates research and development expenses incurred during 2005 and 2004 in each period for our significant groups of research and development projects (in thousands):

Year ended December 31,	2005	2004
GlycoAdvance and GlycoPEGylation	$18,170	$16,650
Other Glycotechnology Programs	978	196
Indirect expenses	13,988	17,826
	$33,136	$34,672

GlycoAdvance and GlycoPEGylation

Our GlycoAdvance and GlycoPEGylation research and development expenses increased during 2005, compared to 2004, primarily due to increased preclinical development costs associated with NE-180 and GlycoPEG-GCSF, and increased purchases of laboratory services and research supplies.

Other Glycotechnology Programs

Research and development expenses related to our Other Glycotechnology Programs increased during 2005, compared to 2004, primarily due to increased research during 2005 to assess opportunities to use our enzymatic technologies in glycolipids.

Indirect expenses

Our indirect research and development expenses decreased during 2005, compared to 2004, primarily due to decreased depreciation resulting from the August 2005 impairment of our San Diego and Witmer Road facilities and their related assets. Further contributing to the decrease during 2005 were lower amounts spent for indirect outside laboratory services and consulting.

General and Administrative Expense. General and administrative expenses for the year ended December 31, 2005 were $10,878,000, compared to $11,711,000 for the corresponding period in 2004. The decrease in 2005 was attributable to lower salaries and personnel-related expenses, lower consulting costs, and reduced depreciation, which resulted from the August 2005 impairment of our San Diego and Witmer Road facilities and their related assets. Partially offsetting these decreases were an increase in patent legal expenses as well as higher non-cash compensation expenses due to the issuance of restricted stock units. During 2006, excluding the effect of the adoption of SFAS No. 123R, we expect our general and administrative expenses to remain relatively consistent with the 2005 expense amounts.

Restructuring Charges. Restructuring charges for the year ended December 31, 2005 were $14,206,000, which included $13,187,000 of non-cash property and equipment impairment charges and $1,019,000 of expected payments for employee severance and facility closure costs. We did not incur any restructuring charges during 2004.

Interest Income. Interest income for the year ended December 31, 2005 was $1,536,000, compared to $652,000 for the corresponding period in 2004. The increase was due to higher interest rates during 2005. Our interest income during 2006 is difficult to project, and will depend largely on prevailing interest rates and whether we enter into any new collaborative agreements and complete any equity or debt financings during 2006.

Interest Expense. Interest expense for the year ended December 31, 2005 was $1,314,000, compared to $981,000 for the corresponding period in 2004, primarily due to higher interest rates during 2005. The increase was also partially attributable to the fact that we did not capitalize any interest expense during 2005. During 2004, we capitalized $139,000 of interest expense associated with leasehold improvements that we placed in service in April 2004. Our interest expense during 2006 is difficult to project and will depend largely on prevailing interest rates, whether we repay debt in connection with any sale of the Witmer Road facility, and whether we complete any new debt financings. See Financing Activities Debt Financing Activities in the Liquidity and Capital Resources section of this Form 10-K for a description of the material features of our debt financings.

Years Ended December 31, 2004 and 2003

Our net loss for the year ended December 31, 2004 was $41,642,000 compared to $37,681,000 for the corresponding period in 2003. The following section explains the trends within each component of net loss for 2004 compared to 2003.

Revenue from Collaborative Agreements. Revenue from collaborative agreements increased to $5,070,000 in 2004 from $1,435,000 in 2003, primarily due to research and development funding under our collaborations with Novo Nordisk and BioGeneriX.

Research and Development Expense. Our research and development expenses increased to $34,672,000 in 2004 from $26,821,000 in 2003. The following table illustrates research and development expenses incurred during 2004 and 2003 in each period for our significant groups of research and development projects (in thousands).

Year ended December 31,	2004	2003
GlycoAdvance and GlycoPEGylation	$ 16,650	$ 10,012
Other Glycotechnology Programs	196	486
Indirect expenses	17,826	16,323
	$ 34,672	$ 26,821

GlycoAdvance and GlycoPEGylation

Our GlycoAdvance and GlycoPEGylation research and development expenses increased during 2004, compared to 2003, primarily due to increased preclinical development costs associated with NE-180 and GlycoPEG-GCSF, 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 2004, compared to 2003, consistent with our focus on our GlycoAdvance and GlycoPEGylation programs.

Indirect expenses

Our indirect research and development expenses increased during 2004, compared to 2003, primarily due to increases related to depreciation of the leasehold improvements at a facility that we occupied in April 2004, as well as the costs associated with operating this facility.

General and Administrative Expense. General and administrative expenses for the year ended December 31, 2004 were $11,711,000, compared to $11,148,000 for the corresponding period in 2003. The 2004 period contained higher patent legal expenses than the comparable 2003 period.

Impairment of Equity Securities. 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 would have been senior to the Series A liquidation preference and exceeded 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. We did not record any impairment charges during 2004.

Interest Income. Interest income for the year ended December 31, 2004 was $652,000, compared to $564,000 for the corresponding period in 2003. The increase was due to higher average cash and cash equivalents balances, as well as slightly higher interest rates, during 2004.

Interest Expense. Interest expense for the year ended December 31, 2004 was $981,000, compared to $461,000 for the corresponding period in 2003, primarily due to higher average debt outstanding during 2004. The increase was partly offset by the capitalization of more interest expense during 2004 than 2003. During 2004 and 2003, we capitalized $139,000 and $42,000, respectively, of interest expense associated with leasehold improvements which we placed in service in April 2004.

Recent Accounting Pronouncements

In May 2005, the Financial Accounting Standards Board (FASB) issued SFAS No. 154, *Accounting Changes and Error Corrections a replacement of APB Opinion No. 20 and FASB Statement No. 3* (SFAS No. 154), which replaces APB Opinion No. 20, *Accounting Changes*, and SFAS No. 3, *Reporting Accounting Changes in Interim Financial Statements*, and changes the requirements for the accounting for and reporting of a change in accounting principle. SFAS No. 154 applies to all voluntary changes in accounting principle, and also applies to changes required by an accounting pronouncement in the unusual instance that the pronouncement does not include specific transition provisions. SFAS No. 154 will be effective for accounting changes and corrections of errors made by us in fiscal years beginning after December 15, 2005. SFAS No. 154 does not change the transition provisions of any existing accounting pronouncements, including those that are in a transition phase as of the effective date of SFAS No. 154. We do not believe the adoption of SFAS No. 154 will have a material impact on our financial statements.

In March 2005, the FASB issued FASB Interpretation No. 47, *Accounting for Conditional Asset Retirement Obligations an interpretation of FASB Statement No. 143* (FIN 47), which requires companies to recognize a liability for the fair value of a legal obligation to perform asset retirement activities that are conditional on a future event if the amount can be reasonably estimated. We adopted the provisions of FIN 47 on December 31, 2005. No conditional asset retirement obligations were recognized and, accordingly, the adoption of FIN 47 had no effect on our financial statements.

In December 2004, the FASB issued SFAS No. 123 (revised 2004), *Share-Based Payment* (SFAS No. 123R). In April 2005, the Securities and Exchange Commission adopted a rule permitting issuers to implement SFAS No. 123R at the beginning of their first fiscal year beginning after June 15, 2005. The statement requires us to measure all employee stock-based compensation awards using a fair value method and to record such expense in our consolidated financial statements. Under the provisions of SFAS No. 123R, we have the choice of adopting SFAS No. 123R using either (a) the modified prospective method, or (b) the modified retrospective method. Beginning January 1, 2006, we adopted the provisions of SFAS No. 123R using the modified prospective transition method whereby compensation cost will be recognized for new awards granted and awards modified, repurchased, and cancelled after January 1, 2006, and for the unvested portion of all awards issued prior to and outstanding at January 1, 2006 at their respective grant date fair values as the remaining requisite service is rendered. Based on the awards outstanding at February 1, 2006, we estimate that the adoption of SFAS No. 123R will result in approximately $2,000,000 to $2,500,000 of increased compensation expense during the year ended December 31, 2006 as compared to the year ended December 31, 2005. The preceding estimate assumes an equal number of shares issuable pursuant to options granted during 2006 as compared to 2005, and assumes the exercise price for options granted during March through December of 2006 equals the average exercise price for all options granted during 2005.

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

Interest Rate Risk

We are exposed to market risk from changes in interest rates. We are currently not engaged in hedging activities and we do not use derivative financial instruments for speculation or trading purposes. We do not believe that our exposure to interest rate risk is material to our results of operations. The analysis below presents the sensitivity of our interest income and expense to selected changes in market interest rates.

The primary objective of our investment activities is to preserve our capital to fund operations and maximize income from our investments without assuming significant risk. We seek the safety of principal and market liquidity by investing in high credit quality institutional money market funds and fixed income securities. 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. Because our investments are short-term in duration, we believe our exposure to interest rate risk is not significant. We held no marketable securities as of December 31, 2005. The approximate principal amount of our investment portfolio as of December 31, 2005 was $37,738,000, and the weighted-average interest rate and interest income earned on the portfolio during 2005 were 3.00% and $1,536,000, respectively. The sensitivity analysis as it relates to our investment activities assumes an instantaneous 100 basis point move in interest rates from their weighted-average levels in 2005. A 100 basis point move up or down in market interest rates would have caused a corresponding change of $514,000 in interest income for 2005.

As of December 31, 2005, the principal components of our debt portfolio were (1) a term loan from a bank for $7,111,000 that accrues interest at a rate equal to the 90-day LIBOR plus 3.00%, (2) tax-exempt Industrial Development Authority bond of $1,000,000 that accrues interest at a rate equal to the 90-day LIBOR plus 1.50%, (3) a term loan from our landlord of $997,000 that accrues interest at a fixed rate of 13.00%, (4) aggregate equipment financing of $5,075,000 that accrues interest at fixed rates ranging from 8.00% to 9.44% and (5) capital lease obligations with a present value of $271,000, for which we imputed interest at fixed rates ranging from 6.20% to 11.51%. Our aggregate interest expense for 2005 was $1,314,000. By modifying the interest expense associated with our variable rate debt, and fixed rate debt entered into during 2005, a 100 basis point move up or down in market interest rates would have caused a corresponding change of $94,000 in interest expense for 2005.

Foreign Exchange Risk

We have entered into some agreements denominated, wholly or partly, in Euros or other foreign currencies, and, in the future, we may enter into additional, significant agreements denominated in foreign currencies. If the values of these currencies increase against the dollar, our costs would increase. 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 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA.

The financial statements and supplementary data required by this item are attached to this Annual Report on Form 10-K beginning on page F-1.

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

None.

ITEM 9A. CONTROLS AND PROCEDURES.

Disclosure 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), as of December 31, 2005. 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 us in reports that we file or submit 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.

Management s Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting. Internal control over financial reporting is defined in Rule 13a-15(f) and 15d-15(f) under the Exchange Act as a process designed by, or under the supervision of, our principal executive and principal financial and accounting officers and effected by our board of directors and management to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles and includes those policies and procedures that:

- pertain to the maintenance of records that in reasonable detail accurately and fairly reflect the transactions and dispositions of our assets;
- provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with U.S. generally accepted accounting principles, and that receipts and expenditures of our company are being made only in accordance with authorizations of our management and board of directors; and
- provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of our assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Projections of any evaluation of effectiveness to future periods are subject to the risks that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2005. In making this assessment, our management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) in *Internal Control-Integrated Framework.* Based on our assessment, our management believes that, as of December 31, 2005, our internal control over financial reporting is effective. In addition, no changes in our internal control over financial reporting have occurred during the three months ended December 31, 2005 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting. The following is the audit report on our assessment of our internal control over financial reporting issued by the company s independent registered public accounting firm.

Report of Independent Registered Public Accounting Firm

The Board of Directors and Stockholders
Neose Technologies, Inc.:

We have audited management s assessment, included in the accompanying Management s Report on Internal Control Over Financial Reporting, that Neose Technologies, Inc. maintained effective internal control over financial reporting as of December 31, 2005, based on criteria established in Internal Control Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO). Neose Technologies, Inc. s management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting. Our responsibility is to express an opinion on management s assessment and an opinion on the effectiveness of Neose Technologies, Inc. s internal control over financial reporting based on our audit.

We conducted our audit in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects. Our audit included obtaining an understanding of internal control over financial reporting, evaluating management s assessment, testing and evaluating the design and operating effectiveness of internal control, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

A company s internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company s internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company s assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

In our opinion, management s assessment that Neose Technologies, Inc. maintained effective internal control over financial reporting as of December 31, 2005, is fairly stated, in all material respects, based on criteria established in Internal Control Integrated Framework issued by COSO. Also, in our opinion, Neose Technologies, Inc. maintained, in all material respects, effective internal control over financial reporting as of December 31, 2005, based on criteria established in Internal Control Integrated Framework issued by COSO.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the balance sheets of Neose Technologies, Inc. as of December 31, 2005 and 2004, and the related statements of operations, stockholders equity and comprehensive loss, and cash flows for each of the years in the three-year period ended December 31, 2005, and our report dated March 6, 2006 expressed an unqualified opinion on those financial statements.

/s/ KPMG LLP
Philadelphia, Pennsylvania
March 6, 2006

ITEM 9B. OTHER INFORMATION.

None.

PART III

ITEM 10. DIRECTORS AND EXECUTIVE OFFICERS OF THE REGISTRANT.

Information concerning directors and executive officers, appearing under the caption Governance of the Company in our Proxy Statement (the Proxy Statement) to be filed with the SEC in connection with our Annual Meeting of Stockholders to be held on May 4, 2006, and information concerning executive officers, appearing under the caption information under the caption Other Matters Section 16(a) Beneficial Ownership Reporting Compliance in the Proxy Statement, are incorporated herein by reference in response to this Item 10.

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 the 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 our best interest. All of our employees were required to certify that they reviewed and understood the Code when they received it during 2003 or upon their later hire date, and are required to renew this certification annually thereafter and when the Code is changed. The Code of Business Conduct and Ethics is intended to comply with Item 406 of the SEC s Regulation S-K and the rules of NASDAQ.

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.

ITEM 11. EXECUTIVE COMPENSATION.

The information contained in the sections titled Executive Compensation and Governance of the Company Compensation of Directors in the Proxy Statement is incorporated herein by reference in response to this Item 11.

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

The information contained in the section titled Stock Ownership of our Directors, Executive Officers and 5% Beneficial Owners in the Proxy Statement is incorporated herein by reference in response to this Item 12.

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS.

The information contained in the section titled Certain Relationships and Related Transactions in the Proxy Statement is incorporated herein by reference in response to this Item 13.

ITEM 14. PRINCIPAL ACCOUNTANT FEES AND SERVICES.

The information contained in the section titled Relationship with Independent Registered Public Accountants in the Proxy Statement is incorporated herein by reference in response to this Item 14.

PART IV

ITEM 15. EXHIBITS AND FINANCIAL STATEMENT SCHEDULES.

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.

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.

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 Number	Description
3.1	Third Amended and Restated Certificate of Incorporation. (Appendix B)(13)
3.2	Second Amended and Restated By-Laws. (Exhibit 3.2)(5)
3.3	Certificate of Designation establishing and designating the Series A Junior Participating Preferred Stock. (Exhibit 3.3)(1)
4.1	See Exhibits 3.1, 3.2, and 3.3 for instruments defining rights of holders of common stock.
4.2	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 4.2)(1)
4.3	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)(2)
4.4	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)(4)
4.5	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)(6)
10.1	Amended and Restated License Agreement, dated as of February 27, 2003, between University of Pennsylvania and Neose Technologies, Inc. (Exhibit 10.1)(7)
10.2	1995 Amended and Restated Stock Option/Stock Issuance Plan, as amended. (Appendix B)(9)
10.3	Employment Agreement, dated March 29, 2002, between C. Boyd Clarke and Neose Technologies, Inc. (Exhibit 10.1)(3)
10.4	Non-Qualified Stock Option Agreement, dated March 29, 2002, between C. Boyd Clarke and Neose Technologies, Inc. (Exhibit 10.2)(3)

10.5	Form of Change of Control Agreement between Neose Technologies, Inc. and Certain Officers. (Exhibit 10.1)(5)
10.6	Tuition Reimbursement Agreement between A. Brian Davis and Neose Technologies, Inc., dated May 24, 2001. (Exhibit 10.44)(2)
10.7	Change of Control Agreement, dated October 7, 2002, between Debra J. Poul and Neose Technologies, Inc. (Exhibit 10.2)(5)
10.8	Agreement of Lease, dated as of February 15, 2002, between Liberty Property Leased Partnership and Neose Technologies, Inc. (Exhibit 10.40)(2)
10.9	Standard Industrial/Commercial Multi-Tenant Lease-Net, dated February 2, 2001, between Nancy Ridge Technology Center, LLC and Neose Technologies, Inc. (Exhibit 10.47)(2)
10.10	First Amendment to Lease, dated May 18, 2001, between Nancy Ridge Technology Center, LLC and Neose Technologies, Inc. (Exhibit 10.48)(2)
10.11	Agreement, dated as of August 24, 2001, between IPS and Neose Technologies, Inc. (Exhibit 10.49)(2)
10.12	Master Security Agreement between General Electric Capital Corporation and Neose Technologies, Inc., dated as of December 19, 2002. (Exhibit 10.33)(7)
10.13	Amendment to Master Security Agreement between General Electric Capital Corporation and Neose Technologies, Inc., dated as of December 19, 2002. (Exhibit 10.34)(7)

Exhibit Number	Description
10.14	Promissory Note of Neose Technologies, Inc. to General Electric Capital Corporation, dated December 27, 2002. (Exhibit 10.35)(7)
10.15	Promissory Note of Neose Technologies, Inc. to General Electric Capital Corporation, dated March 28, 2003. (Exhibit 10.3)(8)
10.16	Promissory Note of Neose Technologies, Inc. to General Electric Capital Corporation, dated September 17, 2003. (Exhibit 10.1)(10)
10.17	Research, Development and License Agreement between Neose Technologies, Inc. and Novo Nordisk A/S dated as of November 17, 2003. (Exhibit 10.39)(11)
10.18	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. (Exhibit 10.40)(11)
10.19	Amendment to Research, Development and License Agreement between Neose Technologies, Inc. and Novo Nordisk A/S dated December 18, 2003. (Exhibit 10.41)(12)
10.20	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. (Exhibit 10.42)(11)
10.21	Promissory Note of Neose Technologies, Inc. to General Electric Capital Corporation, dated December 18, 2003. (Exhibit 10.43)(11)
10.22	Credit Agreement by and between Brown Brothers Harriman & Co. and Neose Technologies, Inc., dated as of January 30, 2004. (Exhibit 10.44)(11)
10.23	General Security Agreement by Neose Technologies, Inc. to Brown Brothers Harriman & Co., dated as of January 30, 2004. (Exhibit 10.45)(11)
10.24	Open-end Mortgage and Security Agreement by and between Neose Technologies, Inc. and Brown Brothers Harriman & Co., dated as of January 30, 2004. (Exhibit 10.46)(11)
10.25	Term Loan Note of Neose Technologies, Inc. to Brown Brothers Harriman & Co., dated January 30, 2004. (Exhibit 10.47)(11)
10.26	Promissory Note of Neose Technologies, Inc. to General Electric Capital Corporation, dated March 30, 2004. (Exhibit 10.1)(12)
10.27	Financing Agreement by and among Montgomery County Industrial Development Authority, Neose Technologies, Inc. and Brown Brothers Harriman & Co., dated February 23, 2004. (Exhibit 10.2)(12)
10.28	

	General Security Agreement by Neose Technologies, Inc. to Brown Brothers Harriman & Co., dated February 23, 2004. (Exhibit 10.3)(12)
10.29	Open-end Mortgage and Security Agreement by and between Neose Technologies, Inc. and Brown Brothers Harriman & Co., dated February 23, 2004. (Exhibit 10.4)(12)
10.30	Research, Co-Development and Commercialization Agreement between BioGeneriX AG and Neose Technologies, Inc., dated April 20, 2004. (Exhibit 10.5)(14)
10.31	Research, Development and License Agreement between Neose Technologies, Inc. and MacroGenics, Inc., dated April 26, 2004. (Exhibit 10.6)(14)
10.32	First Amendment to Lease between Liberty Property Limited Partnership and Neose Technologies, Inc., dated May 18, 2004. (Exhibit 10.7)(14)
10.33	Promissory Note of Neose Technologies, Inc. to Liberty Property Limited Partnership, dated May 7, 2004. (Exhibit 10.8)(14)
10.34	Neose Technologies, Inc. 2004 Equity Incentive Plan. (Appendix C)(13)
10.35	Separation Agreement between Neose Technologies, Inc. and Robert I. Kriebel, dated September 23, 2004 (Exhibit 10.10)(15)
10.36	Promissory Note of Neose Technologies, Inc. to General Electric Capital Corporation dated August 20, 2004. (Exhibit 10.11)(16)
10.37	Form of Incentive Stock Option Award Agreement under the Neose Technologies, Inc. 2004 Equity Incentive Plan. (Exhibit 10.12)(16)

Exhibit Number	Description
10.38	Form of Non-Qualified Stock Option Award Agreement under the Neose Technologies, Inc. 2004 Equity Incentive Plan. (Exhibit 10.13)(16)
10.39	Form of Annual Director Grant Agreement under the Neose Technologies, Inc. 2004 Equity Incentive Plan. (Exhibit 10.14)(16)
10.40	Form of Director Fee Option Grant Agreement under the Neose Technologies, Inc. 2004 Equity Incentive Plan. (Exhibit 10.15)(16)
10.41#	Letter dated October 12, 2004 (effective November 9, 2004) amending Research, Development and License Agreement among Neose Technologies, Inc. and Novo Nordisk A/S and Novo Nordisk Health Care AG dated November 17, 2003, as amended. (Exhibit 10.45)(1)
10.42#	Letter dated October 12, 2004 (effective November 9, 2004) amending Research, Development and License Agreement Between Neose Technologies, Inc. and Novo Nordisk A/S dated as of November 17, 2003, as amended. (Exhibit 10.46)(1)
10.43	Promissory Note of Neose Technologies, Inc. to General Electric Capital Corporation, dated December 16, 2004. (Exhibit 10.47)(1)
10.44	Promissory Note of Neose Technologies, Inc. to General Electric Capital Corporation, dated December 16, 2004. (Exhibit 10.48)(1)
10.45	Form of Restricted Stock Unit Agreement (cliff vesting) between Neose Technologies, Inc. and Certain Employees, Officers and Directors. (Exhibit 10.1)(17)
10.46	Form of Restricted Stock Unit Agreement (quarterly vesting) between Neose Technologies, Inc. and Certain Employees, Officers and Directors. (Exhibit 10.2)(17)
10.47	Letter Agreement dated March 3, 2005 by and between Neose Technologies, Inc and C. Boyd Clarke. (Exhibit 10.3)(17)
10.48#	Letter dated February 16, 2005 amending the Research, Development and License Agreement by and between Neose Technologies, Inc. and Novo Nordisk A/S dated as of November 17, 2003, as amended. (Exhibit 10.2)(18)
10.49#	Research, License and Option Agreement by and between BioGeneriX AG and Neose Technologies, Inc. dated April 28, 2005. (Exhibit 10.1)(19)
10.50	Promissory Note of Neose Technologies, Inc. to General Electric Capital Corporation dated July 12, 2005. (Exhibit 10.1)(20)
10.51*	Separation Agreement between Neose Technologies, Inc. and Joseph J. Villafranca, dated October 31, 2005.
10.52*	

	Separation Agreement between Neose Technologies, Inc. and Marjorie A. Hurley, dated October 31, 2005.
10.53#*	Amendment No. 3 to the Research, Development and License Agreement by and among Neose Technologies, Inc., Novo Nordisk A/S and Novo Nordisk Health Care AG dated December 15, 2005.
23.1*	Consent of KPMG 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 Annual Report on Form 10-K filed with the SEC on March 11, 2005.

(2) Filed as an Exhibit to our Annual Report on Form 10-K filed with the SEC on March 29, 2002.

(3) Filed as an Exhibit to our Current Report on Form 8-K/A filed with the SEC on April 30, 2002.

(4) Filed as an Exhibit to our Current Report on Form 8-K filed with the SEC on June 13, 2002.

(5) Filed as an Exhibit to our Quarterly Report on Form 10-Q for the quarterly period ended September 30, 2002.

(6) Filed as an Exhibit to our Current Report on Form 8-K filed with the SEC on November 1, 2002.

(7) Filed as an Exhibit to our Annual Report on Form 10-K for the year ended December 31, 2002.

(8) Filed as an Exhibit to our Quarterly Report on Form 10-Q for the quarterly period ended March 31, 2003.

(9) Filed as an Exhibit to our Proxy Statement filed with the SEC on April 7, 2003.

(10) Filed as an Exhibit to our Quarterly Report on Form 10-Q for the quarterly period ended September 30, 2003.

(11) Filed as an Exhibit to our Annual Report on Form 10-K for the year ended December 31, 2003.

(12) Filed as an Exhibit to our Quarterly Report on Form 10-Q for the quarterly period ended March 31, 2004.

(13) Filed as an Exhibit to our Proxy Statement filed with the SEC on April 2, 2004.

(14) Filed as an Exhibit to our Quarterly Report on Form 10-Q for the quarterly period ended June 30, 2004.

(15) Filed as an Exhibit to our Current Report on Form 8-K filed with the SEC on September 24, 2004.

(16) Filed as an Exhibit to our Quarterly Report on Form 10-Q for the quarterly period ended September 30, 2004.

(17) Filed as an Exhibit to our Current Report on Form 8-K filed with the SEC on March 4, 2005.

(18) Filed as an Exhibit to our Quarterly Report on Form 10-Q for the quarterly period ended March 31, 2005.

(19) Filed as an Exhibit to our Quarterly Report on Form 10-Q for the quarterly period ended June 30, 2005.

(20) Filed as an Exhibit to our Quarterly Report on Form 10-Q for the quarterly period ended September 30, 2005.

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: March 7, 2006

By: /s/ C. Boyd Clarke

C. Boyd Clarke
Chairman 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 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 C. Boyd Clarke	Chairman and Chief Executive Officer (Principal Executive Officer)	March 7, 2006
/s/ A. Brian Davis A. Brian Davis	Senior Vice President and Chief Financial Officer (Principal Financial and Accounting Officer)	March 7, 2006
/s/ Brian H. Dovey Brian H. Dovey	Director	March 7, 2006
/s/ L. Patrick Gage L. Patrick Gage	Director	March 7, 2006
/s/ William F. Hamilton William F. Hamilton	Director	March 7, 2006
/s/ Douglas J. MacMaster, Jr. Douglas J. MacMaster, Jr.	Director	March 7, 2006
/s/ H. Stewart Parker H. Stewart Parker	Director	March 7, 2006
/s/ Mark H. Rachesky	Director	

Mark H. Rachesky		March 7, 2006
/s/ Lowell E. Sears Lowell E. Sears	Director	March 7, 2006
/s/ George J. Vergis George J. Vergis	Director	March 7, 2006
/s/ Elizabeth H.S. Wyatt Elizabeth H.S. Wyatt	Director	March 7, 2006

Index to Financial Statements

Report of Independent Registered Public Accounting Firm

The Board of Directors and Stockholders
Neose Technologies, Inc.:

We have audited the accompanying balance sheets of Neose Technologies, Inc. as of December 31, 2005 and 2004, and the related statements of operations, stockholders equity and comprehensive loss, and cash flows for each of the years in the three-year period ended December 31, 2005. These financial statements are the responsibility of the management of Neose Technologies, Inc. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (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. as of December 31, 2005 and 2004, and the results of its operations and its cash flows for each of the years in the three-year period ended December 31, 2005, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the effectiveness of Neose Technologies, Inc. s internal control over financial reporting as of December 31, 2005, based on the criteria established in Internal Control Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO), and our report dated March 6, 2006 expressed an unqualified opinion on management s assessment of, and the effective operation of, internal control over financial reporting.

/s/ KPMG LLP
Philadelphia, Pennsylvania
March 6, 2006

Neose Technologies, Inc.
Balance Sheets
(in thousands, except per share amounts)

	December 31, 2005	2004
Assets		
Current assets:		
Cash and cash equivalents	$ 37,738	$ 45,048
Accounts receivable	1,076	2,150
Prepaid expenses and other current assets	892	618
Total current assets	39,706	47,816
Property and equipment, net	24,708	41,133
Intangible and other assets, net	949	1,782
Total assets	$ 65,363	$ 90,731
Liabilities and Stockholders Equity		
Current liabilities:		
Current portion of long-term debt and capital lease obligations	$ 4,031	$ 4,586
Accounts payable	722	1,783
Accrued compensation	1,618	1,916
Accrued expenses	2,697	2,052
Deferred revenue	1,527	1,560
Total current liabilities	10,595	11,897
Long-term debt and capital lease obligations, net of current portion	10,423	13,759
Deferred revenue, net of current portion	3,765	3,688
Other liabilities	463	533
Total liabilities	25,246	29,877
Commitments and contingencies (See Note 14)		
Stockholders equity:		
Preferred stock, par value $.01 per share, 5,000 shares authorized, none issued		
Common stock, par value $.01 per share, 50,000 shares authorized; 32,782 and 24,717 shares issued and outstanding	328	247
Additional paid-in capital	279,015	248,027
Deferred compensation	(6)	(39)
Accumulated deficit	(239,220)	(187,381)
Total stockholders equity	40,117	60,854
Total liabilities and stockholders equity	$ 65,363	$ 90,731

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

Neose Technologies, Inc.
Statements of Operations
(in thousands, except per share amounts)

	Year ended December 31,		
	2005	2004	2003
Revenue from collaborative agreements	$ 6,137	$ 5,070	$ 1,435
Operating expenses:			
Research and development	33,136	34,672	26,821
General and administrative	10,878	11,711	11,148
Restructuring charges	14,206		
Total operating expenses	58,220	46,383	37,969
Operating loss	(52,083)	(41,313)	(36,534)
Other income	22		
Impairment of equity securities			(1,250)
Interest income	1,536	652	564
Interest expense	(1,314)	(981)	(461)
Net loss	$ (51,839)	$ (41,642)	$ (37,681)
Basic and diluted net loss per share	$ (1.64)	$ (1.82)	$ (2.14)
Weighted-average shares outstanding used in computing basic and diluted net loss per share	31,590	22,898	17,611

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

Neose Technologies, Inc.
Statements of Stockholders Equity and Comprehensive Loss
(in thousands)

	Common stock Shares	Amount	Additional paid-in capital	Treasury stock	Deferred compensation	Accumulated deficit	Total stockholders equity
Balance, January 1, 2003	14,324	$ 143	$ 178,945	$ (175)	$ (170)	$ (108,058)	$ 70,685
Net and total comprehensive loss						(37,681)	(37,681)
Sale of common stock in a registered offering	2,655	26	22,351				22,377
Sale of common stock in a private placement	2,867	29	16,291				16,320
Exercise of stock options	63	1	171				172
Shares issued pursuant to employee stock purchase plan	26		21	175			196
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		100
Non-employee options					44		44
Balance, December 31, 2003	19,935	199	217,849		(96)	(145,739)	72,213
Net and total comprehensive loss						(41,642)	(41,642)
Sale of common stock in a registered offering	4,733	47	29,881				29,928
Exercise of stock options	25	1	73				74
Shares issued pursuant to employee stock purchase plan	24		175				175
Deferred compensation related to grants of employee stock options			56		(56)		

Deferred compensation related to non-employee stock options			(8)		8		
Stock-based compensation related to modification of options			1				1
Amortization of deferred compensation related to:							
Employee options					101		101
Non-employee options					4		4
Balance, December 31, 2004	24,717	247	248,027		(39)	(187,381)	60,854
Net and total comprehensive loss						(51,839)	(51,839)
Sale of common stock in a registered offering	8,050	81	29,925				30,006
Shares issued pursuant to employee stock purchase plan	15		86				86
Restricted share units:							
Conversion of liability-classified awards to equity-classified awards			382				382
Compensation cost recognized in the statement of operations			609				609
Deferred compensation related to non-employee stock options			(14)		14		
Amortization of deferred compensation related to:							
Employee options					28		28
Non-employee options					(9)		(9)
Balance, December 31, 2005	32,782	$ 328	$ 279,015	$	$ (6)	$ (239,220)	$ 40,117

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

Neose Technologies, Inc.
Statements of Cash Flows
(in thousands)

	Year ended December 31,		
	2005	2004	2003
Cash flows from operating activities:			
Net loss	$ (51,839)	$ (41,642)	$ (37,681)
Adjustments to reconcile net loss to cash used in operating activities:			
Impairment of property and equipment	13,187	104	
Depreciation and amortization expense	4,322	6,063	4,818
Non-cash compensation expense	628	106	144
Loss (gain) on disposition of equipment and assets held for sale, net	(4)	95	264
Changes in operating assets and liabilities:			
Accounts receivable	1,809	(1,438)	128
Prepaid expenses and other current assets	(150)	330	(487)
Intangible and other assets		47	16
Accounts payable	(1,043)	(559)	1,215
Accrued compensation	84	(594)	708
Accrued expenses	698	411	(200)
Deferred revenue	(691)	213	4,013
Other liabilities	(70)	120	(336)
Net cash used in operating activities	(33,069)	(36,744)	(27,398)
Cash flows from investing activities:			
Purchases of property and equipment	(792)	(9,844)	(3,455)
Proceeds from sale of equipment and assets held for sale	110		
Proceeds from settlement of property and equipment dispute	75		
Purchases of marketable securities	(9,845)		(38,569)
Proceeds from sales of marketable securities			18,219
Proceeds from maturities of marketable securities	10,000	5,000	25,500
Impairment of equity securities			1,250
Net cash provided by (used in) investing activities	(452)	(4,844)	2,945
Cash flows from financing activities:			
Proceeds from issuance of debt	1,484	14,112	4,987
Repayments of debt	(5,365)	(6,552)	(2,584)
Debt issuance costs		(103)	(78)
Restricted funds related to debt		901	76
Proceeds from issuance of common stock, net	30,092	30,177	39,065

Net cash provided by financing activities	26,211	38,535	41,466
Net increase (decrease) in cash and cash equivalents	(7,310)	(3,053)	17,013
Cash and cash equivalents, beginning of year	45,048	48,101	31,088
Cash and cash equivalents, end of year	$ 37,738	$ 45,048	$ 48,101

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

Neose Technologies, Inc.
Notes to Financial Statements
(in thousands, except per share amounts)

Note 1. Background

We are a biopharmaceutical company using our enzymatic technologies to develop proprietary drugs, focusing primarily on therapeutic proteins. We believe that our core enzymatic technologies, GlycoAdvance® and GlycoPEGylation , improve the drug properties of therapeutic proteins by building out, and attaching polyethylene glycol (PEG) to, carbohydrate structures on the proteins. We are using our technologies to develop proprietary versions of protein drugs with proven safety and efficacy and to improve the therapeutic profiles of proteins being developed by our partners. We expect these modified proteins to offer significant advantages, including less frequent dosing and possibly improved efficacy, over the original versions of the drugs now on the market, as well as to meet or exceed the pharmacokinetic profile of next-generation versions of the drugs now on the market. We believe this strategy of targeting drugs with proven safety and efficacy allows us to lower the risk profile of our proprietary development portfolio as compared to *de novo* protein drug development.

We have incurred losses each year since inception. As of December 31, 2005, we had an accumulated deficit of $239,220. We 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, and expand our business development and commercialization efforts. Given our planned level of operating expenses, we expect to continue incurring losses for some time. We believe that our existing cash and cash equivalents, expected revenue from collaborations and license arrangements, and interest income should be sufficient to meet our operating and capital requirements at least through 2006, although changes in our collaborative relationships or our business, whether or not initiated by us, may cause us to deplete our cash and cash equivalents sooner than the above estimate. We will require significant amounts of additional capital in the future to fund our operations, 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. If we are unable to raise additional capital when required, we may need to delay, scale back, or eliminate some of our research and development programs.

We have not yet developed any products or commercialized any products or technologies, and we may never be able to do so. 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. Our operations are subject to risks and uncertainties other than mentioned above including, among others, the uncertainty of product development, including our limited product development and manufacturing experience; our dependence upon collaborative partners to develop and commercialize products incorporating our technologies and the success of collaborative relationships; the uncertainty of intellectual property rights; technological uncertainty and the risk of technological obsolescence; the risk of development and commercialization of competitive products by others that are more effective, less costly, or otherwise gain greater market acceptance; and the uncertainty of achieving regulatory approvals for our products, or products incorporating our technologies.

Our revenue from collaborative agreements increased from $1,435 in the year ended December 31, 2003 to $5,070 in the year ended December 31, 2004. In April 2005, we entered into an agreement with BioGeneriX AG for the use of our GlycoAdvance® and GlycoPEGylation technologies to develop a long-acting version of a currently marketed therapeutic protein (see Note 11). We have partnered five of the six proprietary drug programs that use our technologies and are in various stages of research and preclinical development. We have an additional two proteins available for partnering. Under our collaborative agreements, we have begun to receive significant revenues from our planned principal operation of developing proprietary drugs. As a result of the revenue growth in the year ended December 31, 2004 compared to the year ended December 31, 2003 and because we entered into new collaborative agreements in 2004 and 2005, we are no longer considered a development-stage company as we had been since our inception in January 1989, and all cumulative information reported in prior years is no longer reported.

Neose Technologies, Inc.
Notes to Financial Statements
(in thousands, except per share amounts)

Note 2. Summary of Significant Accounting Policies

Use of Estimates

The preparation of financial statements, in conformity with U.S. generally accepted accounting principles, 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, 2005 and 2004, cash equivalents consisted of securities and obligations of either the U.S. Treasury or U.S. government agencies and money market investments. Our cash balances have been kept on deposit primarily at one bank and in amounts greater than $100, 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, 2005 and 2004, we held no marketable securities. Securities maturing during the years ended December 31, 2005, 2004 and 2003 earned interest of $155, $55, and $310, respectively.

During 2003, securities that were classified as held-to maturity were sold before the maturity date due to an error by the then-custodian of our investment account. We received proceeds of $18,219 from the sales of the securities, which had an aggregate amortized cost of $18,213, and realized a gain of $6.

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. Expenditures for additions and improvements are capitalized, while maintenance and repairs are charged to expense as incurred. Depreciation and amortization are calculated using the straight-line method over the estimated useful lives of the assets. Buildings are depreciated over 20 years, while laboratory, manufacturing, and office equipment are depreciated over three to seven years. For assets acquired under capital leases and for leasehold improvements, depreciation and amortization are calculated on the straight-line method over the estimated useful lives of the assets or the lease term, whichever is shorter. Upon the disposition of assets, the cost and related accumulated depreciation are removed from the accounts and any resulting gain or loss is included on our statements of operations.

Neose Technologies, Inc.
Notes to Financial Statements
(in thousands, except per share amounts)

Impairment of Long-Lived Assets

Long-lived assets and certain identifiable intangibles are reviewed for impairment at least annually and whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable. Recoverability of assets held and used is measured by a comparison of the carrying amount of an asset to future net undiscounted cash flows expected to be generated by the asset. If such assets are considered to be impaired, the impairment to be recognized is measured by the amount by which the carrying amount of the assets exceeds the fair value of the assets. Assets to be disposed of are reported at the lower of the carrying amount or fair value less costs to sell. As described in Note 5, we recognized during the third quarter of 2005 non-cash impairment charges on our property and equipment as a result of the restructuring we announced in August 2005 (see Note 12). Because our history of negative operating cash flows is an indicator of impairment, we annually compare the market value of our equity and debt to the carrying value of our net assets. The market value of our equity and debt exceeded the carrying value of our net assets as of December 31, 2005 and, therefore, we did not recognize any impairment of long-lived assets other than the impairment recorded in connection with our August 2005 restructuring.

Financing Costs Related to Long-term Debt

Costs associated with obtaining long-term debt are deferred and amortized to interest expense over the term of the related debt.

Revenue Recognition

Revenue from collaborative agreements consists of upfront fees, research and development funding, and milestone payments. Upfront fees and payments received from non-substantive milestones, such as the passage of time, 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 substantive 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. 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 consulting and contract research, development, and manufacturing 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.

Some of our research and development is conducted by third parties, including contract research and development service providers. At the end of each quarter, we compare the payments made to each service provider to the estimated progress toward completion of the research or development objectives. Such estimates are subject to change as additional information becomes available. Depending on the timing of payments to the service providers and the estimated service provided, we may record net prepaid or accrued expense relating to these costs. We monitor each of these factors to the extent possible and adjust estimates accordingly.

Accounting for Restructuring Costs

In August 2005, we implemented a restructuring of operations (see Note 12). Statement of Financial Accounting Standards (SFAS) No. 146, *Accounting for Costs Associated with Exit or Disposal Activities* (SFAS No. 146), addresses financial accounting and reporting for costs associated with exit or disposal activities. SFAS No. 146

Neose Technologies, Inc.
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requires a liability for a cost associated with an exit or disposal activity be recognized and measured initially at fair value only when the liability is incurred. SFAS No. 146 does not apply to costs associated with a disposal activity covered by SFAS No. 144, *Accounting for the Impairment or Disposal of Long-Lived Assets* (SFAS No. 144). The restructuring charges recorded by us during 2005 were comprised primarily of costs to reduce property and equipment to fair value and to reduce our workforce.

Under SFAS No. 144, any impairment of property and equipment to be recognized is measured by the amount by which the carrying amount of the assets exceeds the fair value of the assets. To determine the fair value of assets that are not likely to be used over their remaining useful economic life, we use a probability-weighted approach of estimated cash flows to be received upon a range of possible disposition outcomes. In August 2005, we announced we would evaluate for our current headquarters and pilot manufacturing facility (Witmer Road facility), which we own subject to a mortgage, including the potential disposition of the facility and further consolidation of our research, development and administrative operations into a currently leased facility also located in Horsham, Pennsylvania. As a result of the announcement, we concluded that identifiable cash flows could be assigned to the Witmer Road facility and related equipment. We based our estimates of potential cash flows related to possible disposition outcomes on conversations with commercial real estate firms that have both knowledge of recent history of sales and expertise in marketing and selling similar facilities. These estimates may turn out to be incorrect and our actual cash flows may be materially different from our estimates.

Under SFAS No. 146, any employee severance costs are determined based on the estimated severance and fringe benefit charge for identified employees. In calculating the cost to exit facilities, we estimate the future lease and operating costs to be paid until the lease is terminated, the amount, if any, of sublease receipts, and real estate broker fees. This requires us to estimate the timing and costs of the amount of operating costs and the timing and rate at which we might be able to sublease the site. To form our estimates for these costs, we performed an assessment of the affected facility and considered the current market conditions, if any. Our assumptions on operating costs until terminated and offsetting sublease receipts, if any, may turn out to be incorrect and our actual costs may be different from our estimates.

Our estimates of future liabilities may change, requiring us to record additional restructuring charges or reduce the amount of liabilities recorded. At the end of each reporting period, we evaluate the remaining accrued restructuring charges to ensure their adequacy, that no excess accruals are retained and the utilization of the provisions are for their intended purposes in accordance with developed exit plans. We periodically evaluate current available information and adjust our accrued restructuring charges as necessary.

Interest Expense

During each of the two years ended December 31, 2004, we incurred significant capital expenditures related to improving our owned and leased facilities. See Note 5 for a description of our property and equipment. Accordingly, we capitalized a portion of interest incurred during each reporting period in accordance with SFAS No. 34, *Capitalization of Interest Cost*, as amended. We did not capitalize any interest incurred during the year ended December 31, 2005.

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

Neose Technologies, Inc.
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(in thousands, except per share amounts)

enactment date. We provide a valuation allowance for the full amount of our net deferred tax assets because there is no assurance they will be realized.

Stock-based Employee Compensation

We apply the intrinsic value method of accounting for all stock-based employee compensation in accordance with Accounting Principles Board (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 SFAS 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 SFAS 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:

	Year ended December 31,		
	2005	2004	2003
Net loss as reported			