NEOSE TECHNOLOGIES INC
Form 424B5
February 18, 2005

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Filed pursuant to Rule 424(b)(5)
Registration Number 333-121112

PROSPECTUS SUPPLEMENT

(To Prospectus dated January 10, 2005)

7,000,000 Shares

Common Stock

We are offering all of the 7,000,000 shares of common stock offered by this prospectus supplement.

Our common stock is listed on The NASDAQ National Market under the symbol NTEC. On February 17, 2005, the last reported sale price of our common stock on The NASDAQ National Market was $4.76 per share.

Investing in our common stock involves a high degree of risk. Before buying any shares, you should carefully read the discussion of material risks of investing in our common stock under the heading Risk factors beginning on page S-9 of this prospectus supplement.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus supplement or the accompanying prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

	Per share	Total
Public offering price	$4.00	$28,000,000
Underwriting discounts and commissions	$0.24	$ 1,680,000
Proceeds, before expenses, to us	$3.76	$26,320,000

The underwriters may also purchase up to an additional 1,050,000 shares of our common stock at the public offering price, less underwriting discounts and commissions payable by us, to cover over-allotments, if any, within 30 days of the date of this prospectus supplement. If the underwriters exercise the option in full, the total underwriting discounts and commissions will be $1,932,000, and the total proceeds, before expenses, to us will be $30,268,000.

The underwriters are offering the shares of our common stock as set forth under Underwriting. Delivery of the shares of common stock will be made on or about February 24, 2005.

Sole Book-Running Manager

UBS Investment Bank **JPMorgan**

Jefferies & Company, Inc.

The date of this prospectus supplement is February 18, 2005.

You should rely only on the information contained or incorporated by reference in this prospectus supplement and the accompanying prospectus. We have not, and the underwriters have not, authorized anyone to provide you with additional or different information. We are not making an offer of these securities in any jurisdiction where the offer is not permitted. You should assume that the information in this prospectus supplement is accurate only as of the date on the front of this document and that any information we have incorporated by reference is accurate only as of the date of the document incorporated by reference, regardless of the time of delivery of this prospectus supplement and the accompanying prospectus or of any sale of our common stock.

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Prospectus supplement summary

This summary highlights information contained elsewhere or incorporated by reference in this prospectus supplement and the accompanying prospectus. This summary does not contain all of the information that you should consider before investing in our common stock. You should carefully read the entire prospectus supplement and the accompanying prospectus, including the Risk factors section in this prospectus supplement, as well as the financial statements and the other information incorporated by reference herein before making an investment decision.

Unless the context requires otherwise, the words Neose, we, company, us and our refer to Neose Technologies, Inc.

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. During the second quarter of 2005, we plan to have a pre-Investigational New Drug application (IND) meeting with the U.S. Food and Drug Administration (FDA) and submit an IND to the FDA for NE-180. 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. Prior to the end of 2005, in collaboration with our partner, BioGeneriX, we plan to request scientific advice from regulatory authorities in the European Union (EU) and submit the equivalent of an IND in an EU country for GlycoPEG-GCSF. In 2003, the EPO and G-CSF drug categories had aggregate worldwide sales of approximately $9.7 billion and $3.0 billion, respectively.

Market opportunity

Worldwide sales of protein drugs in 2003 have been reported at approximately $40 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.

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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 and thus compromise 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 multiple 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,

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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 expect to complete various preclinical activities for NE-180, including having a pre-IND meeting with the FDA and submitting an IND to the FDA, during the second quarter of 2005. Our goal is to initiate clinical trials during the third quarter of 2005. We expect that data from these trials will be included in data submitted to the appropriate government agencies for regulatory approval.

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 2003 were approximately $9.7 billion. Of these sales, approximately $6.2 billion were in the U.S., approximately $2.7 billion were in Europe, and approximately $0.8 billion were in Japan.

Based on early 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 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 $4.5 billion during the period from its launch in 2001 through the fourth quarter of 2004.

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 we believe the key blocking patents expire sooner. We believe that the key patents in Europe and Japan will expire by the end of 2005.

In the U.S., we believe that the key patents surrounding EPO will expire by the end of 2015. However, many of the applicable patent claims in the U.S. apply to EPO expressed in vertebrate or mammalian cells, and we believe that our use of an insect cell expression system may allow us to enter the U.S. market prior to the expiration of these patents. 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 and BioGeneriX plan to complete preclinical development activities for GlycoPEG-GCSF prior to the end of 2005, including requesting scientific advice from regulatory authorities in the EU and submitting the equivalent of an IND in an EU country.

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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 2003 were approximately $3.0 billion. Of these sales, approximately $2.0 billion were in the U.S., approximately $0.6 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 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 $3.5 billion during the period from its launch in 2002 through the fourth quarter of 2004.

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 the EU.

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 and BioGeneriX is responsible for supplying the protein and funding the entire clinical development program. 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 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. 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

In January 2005, we entered into a supply and option agreement with BioGeneriX that provides for BioGeneriX to make a non-refundable payment to Neose and to supply to Neose a marketed therapeutic protein (target protein) for research purposes. During a three-month research period, BioGeneriX has an exclusive option to enter into a pre-negotiated research, license and option agreement (license agreement) for the use of our proprietary GlycoAdvance and GlycoPEGylation

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technologies to develop a long-acting version of the target protein. If BioGeneriX exercises the option to enter into the license agreement, Neose would receive an additional non-refundable payment as well as research payments, and could receive milestone payments totaling up to $61.5 million, as well as significant royalties on product sales. The license agreement contemplates that Neose would conduct research on behalf of BioGeneriX for approximately 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, Neose will provide, and be fully reimbursed for, any required technical assistance. BioGeneriX would have the right to terminate the license agreement any time after the research period. Neose would have the right to terminate the license agreement if specific development milestones were 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 $51.3 million in development milestones, 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 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 remodeled compounds into development. During the research phase, we and MacroGenics each fund our own expenses. If MacroGenics decides to proceed with any of the remodeled 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 improve the therapeutic profiles of glycoproteins being developed by our partners. We also plan to 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. We expect to complete preclinical activities for NE-180, including having a pre-IND meeting with the FDA and submitting an IND to the FDA, in the second quarter of 2005. We expect to complete preclinical activities for GlycoPEG-GCSF, including requesting scientific advice from the regulatory authorities in a country in the EU and submitting the equivalent of an IND in an EU country, by the end of 2005 in collaboration with our partner, BioGeneriX.

- **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 profile of

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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 several 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. In addition, we intend to explore the application of our technology and our development capabilities to glycopeptides and antibodies. 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 significantly participate in the commercial success of each of the compounds. This will be accomplished by not only securing upfront payments, research funding and milestone payments, but by continuing to seek agreements that retain meaningful commercial rights in certain territories and securing significant royalty rates on product sales in other territories.

OUR CORPORATE INFORMATION

We were incorporated in Delaware in May 1991. Our principal executive offices are located at 102 Witmer Road, Horsham, PA 19044, and our telephone number is 215-315-9000. We maintain an Internet website at *http://www.neose.com.* We have not incorporated by reference into this prospectus supplement or the accompanying prospectus the information in, or that can be accessed through, our website, and you should not consider it to be a part of this prospectus supplement or the accompanying prospectus.

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The offering

Common stock we are offering	7,000,000 shares
Common stock to be outstanding after this offering	31,732,372 shares
Use of proceeds	We estimate that the net proceeds to us from this offering after deducting underwriting discounts and commissions and the estimated offering expenses will be approximately $25.8 million, or approximately $29.8 million if the underwriters exercise their over-allotment option in full. We intend to use the net proceeds from this offering to fund ongoing research and development activities, general and administrative expenses, capital expenditures, and general working capital. See Use of proceeds.
NASDAQ National Market symbol	NTEC

The number of shares of our common stock outstanding after this offering is based on approximately 24,732,372 shares outstanding as of February 17, 2005 and excludes:

- 4,966,329 shares of our common stock issuable upon exercise of options outstanding as of February 17, 2005, at a weighted average exercise price of $17.11 per share, of which options to purchase 3,322,014 shares were exercisable as of that date at a weighted average exercise price of $18.25 per share; and

- 1,591,794 shares of our common stock available for future grant under our 2004 Equity Incentive Plan as of February 17, 2005.

Unless we specifically state otherwise, the information in this prospectus supplement assumes that the underwriters do not exercise their option to purchase up to 1,050,000 shares of our common stock to cover over-allotments, if any.

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Summary financial data

The following summary financial data for the years ended December 31, 2001 through 2003 is derived from our audited financial statements. The following summary financial data as of September 30, 2004 and for the nine-month periods ended September 30, 2003 and 2004 is derived from our unaudited interim condensed financial statements. The unaudited financial statement data include, in our opinion, all adjustments (consisting only of normal recurring adjustments) that are necessary for a fair presentation of our financial position and results of operations for these periods. Operating results for the nine months ended September 30, 2004 are not necessarily indicative of the results that may be expected for the year ended December 31, 2004.

This information is only a summary and should be read together with the financial statements, the related notes and other financial information incorporated by reference into this prospectus supplement and the accompanying prospectus and on file with the SEC. For more details on how you can obtain our SEC reports incorporated by reference into this prospectus supplement and the accompanying prospectus, see Additional information in the accompanying prospectus.

	Year ended December 31,			Nine months ended September 30,	
Statement of operations data:	**2001**	**2002**	**2003**	**2003**	**2004**
(In thousands, except per share amounts)				**(unaudited)**	
Revenue from collaborative agreements	$ 1,266	$ 4,813	$ 1,435	$ 871	$ 3,592
Operating expenses:					
Research and development	14,857	21,481	26,821	19,031	24,971
Marketing, general and administrative	9,374	12,510	11,148	8,657	9,047
Total operating expenses	24,231	33,991	37,969	27,688	34,018
Operating loss	(22,965)	(29,178)	(36,534)	(26,817)	(30,426)
Other income	6,120	1,653			
Impairment of equity securities			(1,250)	(1,250)	
Interest income	3,704	1,108	564	420	431
Interest expense	(188)		(461)	(338)	(658)
Net loss	$(13,329)	$(26,417)	$(37,681)	$(27,985)	$(30,653)
Basic and diluted net loss per share	$ (0.95)	$ (1.85)	$ (2.14)	$ (1.66)	$ (1.38)
Weighted average shares outstanding used in computing basic and diluted net loss per share	14,032	14,259	17,611	16,828	22,284

	September 30, 2004	
Balance sheet data:	**Actual**	**As adjusted[1]**
(In thousands)	**(unaudited)**	

Cash and cash equivalents	$ 55,016	$ 80,836
Total assets	101,080	126,900
Total debt and capital lease obligations	17,725	17,725
Deficit accumulated during development stage	(176,392)	(176,392)
Total stockholders equity	71,829	97,649

(1) As adjusted to give effect to the sale of 7,000,000 shares of common stock we are offering pursuant to this prospectus supplement, after deducting underwriting discounts and commissions and estimated offering expenses to be paid by us.

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Risk factors

Investing in our common stock involves a high degree of risk. You should consider carefully the risk factors described below and all other information contained in or incorporated by reference in this prospectus supplement and the accompanying prospectus before deciding to invest in our common stock. If any of the following risks actually occurs, it may materially harm our business, financial condition, operating results and cash flow. As a result, the market price of our common stock could decline, and you could lose all or part of your investment. Additional risks and uncertainties that are not yet identified or that we think are immaterial may also materially harm our business, operating results and financial condition and could result in a complete loss of your investment.

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 our existing collaborations and license arrangements, and interest income should be sufficient to meet our operating and capital requirements through 2005, 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 obtaining or manufacturing 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; and
- our need or decision to acquire or license complementary technologies or new drug targets.

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.

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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 entered into a credit agreement with a bank, dated as of January 30, 2004, under which the outstanding balance, as of September 30, 2004, was $9.0 million. Under the credit agreement, 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 September 30, 2004, our total outstanding debt was $17.7 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.

Under our credit agreement, 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 credit agreement. Under the credit agreement, if we fail at any time to maintain a minimum required cash and short-term investments balance of at least $22.0 million, or at any time after January 30, 2008, the bank has 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, which may have the effect of requiring us to repay the then outstanding loan balance under the credit agreement. As of September 30, 2004, we maintained a cash and cash equivalents balance of $55.0 million.

The credit agreement also contains 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 credit agreement could result in a default under our credit agreement. Upon the occurrence of such an event of default, the bank could elect to declare all amounts outstanding thereunder 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 $13.3 million for the year ended December 31, 2001, $26.4 million for the year ended December 31, 2002, $37.7 million for the year ended December 31, 2003, and $30.7 million for the nine months ended September 30, 2004.

Given our planned level of operating expenses, we expect to continue incurring losses for some time. As of September 30, 2004, we had an accumulated deficit of approximately $176.4 million. To date, we have derived substantially all of our revenue from corporate collaborations, license agreements and investments. We expect that substantially all of our revenue for the foreseeable future will result from these sources and from the licensing of our technologies. We also expect to spend significant amounts to expand our research and development on our proprietary drug candidates and technologies, maintain and expand our intellectual property position, expand our manufacturing scale-up activities and expand our business development and commercialization efforts. 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.

Failure to comply with the new SEC rules regarding internal controls over financial reporting by the deadline for compliance could have a material adverse effect on our stock price.

Beginning with our annual report for the year ended December 31, 2004, Section 404 of the Sarbanes-Oxley Act of 2002 will require us to include a report by our management on our internal controls over financial reporting. This report must contain an assessment by management of the effectiveness of our internal controls over financial reporting as of the end of our fiscal year and a statement as to whether or not our internal controls are effective. The report must also contain a statement that our independent auditors have issued an attestation report on management s assessment of such internal controls. Because this is the first annual report to be filed by us requiring this additional information pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, neither we nor our independent auditors have previously performed an evaluation of our internal controls over financial reporting under these new rules. If we are unable to assert that our internal controls over financial reporting are effective, or if our independent auditors are unable to attest that our management s report is fairly stated or they are unable to express an opinion on our management s evaluation or on the effectiveness of our internal controls, the market price of our common stock could be adversely affected.

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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 remodeling 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 one marketed EPO product of a competitor was associated with pure red cell aplasia in post-marketing surveillance studies. This highlights the fact that even after a product is approved for marketing, problems may arise which can negatively affect sales and increase costs.

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.

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 the intended activity 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 the commencement of 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 created 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 EU. 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 manufacturing 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 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 the EPO protein that we are currently manufacturing to support preclinical and early clinical development of NE-180. Our success with this program will depend on our ability to manufacture this protein, at commercial scale, in the insect cell

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expression system (the production source of NE-180), either independently or with 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 date, no product produced in this expression system has received marketing authorization in the U.S. or the EU, which means that we may face previously unidentified problems resulting from the use of this expression system and related regulatory challenges.

We are also manufacturing, directly or through suppliers, the enzymes, sugar nucleotides and other reagents we need to apply our technologies. We have sought and continue to have collaborators, licensees or contract manufacturers manufacture at least some of the compounds necessary to commercialize our technologies. We may not be able to find parties willing and able to manufacture these compounds at acceptable prices, 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 manufacture these compounds on a commercial scale or to obtain commercial quantities, in either case, at reasonable cost. Our manufacturing processes also must comply with current Good Manufacturing Practices, or cGMP, prescribed by the FDA. We may not be able to manufacture or obtain sufficient quantities of the products we develop to meet our needs for pre-clinical or clinical development, and we may have problems complying, or maintaining compliance, with cGMP.

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

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

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- continued consolidation in our target markets may limit our ability to enter into collaboration agreements, or may result in terminations of existing collaborations.

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

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

We may be exposed to product liability and related risks.

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

RISKS RELATED TO INTELLECTUAL PROPERTY

Blocking patents or claims of infringement may stop or delay our 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. As we seek to develop next-generation proprietary products, we devote significant resources to investigating the patent protection surrounding our target proteins. Patent protection for therapeutic proteins often comprises numerous claims for composition of matter, methods of use, and methods of making. The numerous patents 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.

We rely on certain exemptions and safe harbors in order to conduct the necessary research and development to support our regulatory filings. The Supreme Court of the United States has recently agreed to hear a case related to a particular safe harbor upon which we rely in the U.S. The elements of this safe harbor could be modified by the Supreme Court in a manner that is adverse to us, causing an increase in challenges or claims of infringement against us in relation to the patents of third parties and the possibility of our products being blocked from development in the U.S.

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

- the pending patent applications we have filed or to which we have exclusive rights may not result in issued patents or may take longer than we expect to result in issued patents;
- we may be subject to interference proceedings;
- we may be subject to opposition proceedings in foreign countries;
- the claims of any patents that are issued may not provide meaningful protection;
- we may not be able to develop additional proprietary technologies that are patentable;
- the patents licensed or issued to us or our customers may not provide a competitive advantage;
- other companies may challenge patents licensed or issued to us or our customers;
- other companies may independently develop similar or alternative technologies, or duplicate our technologies;
- other companies may design around technologies we have licensed or developed; and
- enforcement of patents is complex, uncertain and expensive.

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.

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.

International patent protection is uncertain.

In addition to the issues discussed under the two preceding risks, patent law outside the U.S. differs from country to country. The laws of some foreign countries may not protect our intellectual property rights to the same extent as U.S. laws. We may participate in opposition proceedings to determine the validity of foreign patents belonging to us or our competitors, which proceedings could result in substantial costs and diversion of our efforts. Finally, some of our patent protection in the U.S. is not available to us in foreign countries due to the differences in the patent laws of those countries.

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

We have licensed patents and patent applications from a number of institutions. Some of our proprietary rights have been licensed to us under agreements that have performance requirements or other contingencies. The failure to comply with these provisions could lead to termination or modifications of our rights to these licenses. Additionally, we may need to obtain additional licenses to patents or other proprietary rights from other parties to facilitate development of our proprietary technology base. 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, Enzon Pharmaceuticals, 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, Transkaryotic Therapeutics, Human Genome Sciences, Maxygen, ARIAD Pharmaceuticals and Affymax. 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.

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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 remodeling our target proteins or the target proteins of our potential collaborators.

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

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

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

Because of the specialized scientific nature of our business, we are highly dependent upon qualified scientific, technical and managerial personnel, including our research and development team and our president, CEO and Chairman, C. Boyd Clarke. The advancement of our business is dependent upon our management team s ability to evaluate collaboration opportunities and on our CEO s ability to focus the Company s efforts. Our anticipated research and development efforts will require additional expertise and the addition of new qualified personnel. There is intense competition for qualified management and research and development personnel in the pharmaceutical field. Therefore, we may not be able to attract and retain the qualified personnel necessary for 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, our ability to manage day-to-day operations, attract collaboration partners, attract and retain other employees, and generate revenues. We do not maintain key man life insurance on any of our employees.

RISKS RELATED TO GOVERNMENT REGULATION

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

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 compound for human use produced in this expression system has been submitted for marketing authorization in the U.S. or EU, 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 would be subject to continued review by the FDA and other regulatory authorities. Any later discovery of unknown problems with our products, products incorporating our technologies, or manufacturing processes could result in restrictions on such products or manufacturing processes, including potential withdrawal of the products from the market. In addition, if regulatory authorities determine that we 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

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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 THE ENVIRONMENT, FACILITIES AND BUSINESS INTERRUPTION

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.

RISKS RELATED TO FOREIGN EXCHANGE

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.

RISKS RELATED TO THE OFFERING

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. Since February 1, 2004, the price of our common stock has traded as high as $12.86 per share in February 2004 and as low as $4.76 per share in February 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.

The ability of our stockholders to control our policies and effect a change of control of our company is limited, which may not be in the best interests of our stockholders.

There are provisions in our certificate of incorporation and bylaws that may discourage a third party from making a proposal to acquire us, even if some of our stockholders might consider the proposal to be in their best interests. For example, our certificate of incorporation authorizes our board of directors to issue shares of preferred stock without stockholder approval and to establish the preferences and rights of any preferred stock issued, which would allow the board to issue one or more classes or series of preferred stock that could discourage or delay a tender offer or change in control. In addition, our board of directors approved on September 17, 1997 a stockholders rights plan, which could prevent or deter a potential unsolicited takeover of us by causing substantial dilution of an acquirer of 15% or more of our outstanding common stock, subject to certain exceptions contained in amendments to the stockholders rights plan. We are also subject to the business combination provisions of Section 203 of the Delaware General Corporation Law, which, in general, imposes restrictions upon acquirers of 15% or more of our stock. As a result, it is difficult for a third party to acquire control of us without the approval of the board of directors and, therefore, mergers and acquisitions of us that our stockholders may consider in their best interests may not occur.

Because we do not intend to pay dividends, stockholders will benefit from an investment in our common stock only if it appreciates in value.

We have never declared or paid any cash dividends on our common stock. We currently intend to retain our future earnings, if any, to finance the expansion of our business and do not expect to pay any cash dividends 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. As a result, the success of an investment in our common stock will depend entirely upon any future appreciation.

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There is no guarantee that our common stock will appreciate in value or even maintain the price at which stockholders have purchased their shares.

New investors in our common stock will experience immediate and substantial dilution.

The offering price of our common stock will be substantially higher than what the net tangible book value per share of our common stock will be immediately after the offering. As a result, purchasers of our common stock in this offering will incur immediate and substantial dilution of $0.98 per share of common stock. Those purchasers will experience additional dilution upon the exercise of outstanding stock options having an exercise price less than the per share offering price to the public in this offering. See Dilution for a more detailed discussion of the dilution new investors will incur in this offering.

Management may invest or spend the proceeds of this offering in ways with which you may not agree and in ways that may not yield a return to our stockholders.

We will retain broad discretion over the use of proceeds from this offering. Stockholders may not deem such uses desirable, and our use of the proceeds may not yield a significant return or any return at all for our stockholders. We expect to use the net proceeds from this offering to fund our research and development activities, general and administrative expenses, capital expenditures and general working capital. A number of variables will influence our actual use of the proceeds from this offering, and our actual uses of the proceeds of this offering may vary substantially from our currently planned uses. Pending the use of the net proceeds, we intend to invest the net proceeds from this offering in short-term, investment grade, interest-bearing securities.

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Special note regarding forward-looking statements

Some of the statements in the sections entitled Prospectus supplement summary and Risk factors and elsewhere in this prospectus supplement and accompanying prospectus, including the documents incorporated herein by reference, contain forward-looking statements within the meaning of Section 27A of the Securities Act. When used in this prospectus supplement, the accompanying prospectus and the documents incorporated herein by reference, the words anticipate, believe, estimate, may, expect, intend, should, plan, will, predict, pot negative of such terms and similar expressions are generally intended to identify forward-looking statements. These forward-looking statements include, among others, the statements about our:

- estimate of the length of time that our existing cash and cash equivalents, expected revenue, and interest income will be adequate to finance our operating and capital requirements;
- 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, manufacture 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 initiation of clinical trials, for NE-180 and GlycoPEG-GCSF;
- expectations for the development of long-acting versions of EPO and G-CSF, and subsequent proprietary drug candidates;
- expectations for incurring additional capital expenditures for renovations of our facilities;
- 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.

Our actual results could differ materially from the results expressed in, or implied by, these 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;
- 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;
- our ability to develop and commercialize products without infringing the patent or intellectual property rights of others;

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

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Special note regarding forward-looking statements

- our and our collaborators ability to develop and commercialize therapeutic proteins and our ability to commercialize our technologies;
- our ability to compete successfully in an intensely competitive field;
- our ability to renovate our facilities as required for our operations;
- our ability to attract and retain key personnel; and
- general economic conditions.

These and other risks and uncertainties that could affect our actual results are discussed in this prospectus supplement and accompanying prospectus, particularly in the section of this prospectus supplement entitled Risk factors, and in our other filings with the SEC.

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 prospectus to conform them to actual results, except as required by the federal securities laws.

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Use of proceeds

We estimate that the net proceeds from the sale of the 7,000,000 shares of common stock we are offering will be approximately $25.8 million, after deducting underwriting discounts and commissions and the estimated offering expenses payable by us. If the underwriters exercise their over-allotment option in full, we estimate the net proceeds to us will be approximately $29.8 million.

We intend to use the net proceeds for:

- ongoing research and development activities, including process development and the conduct of preclinical and clinical trials for our proprietary protein product candidates;
- general and administrative expenses;
- capital expenditures; and
- general working capital.

Although we have identified some of the potential uses of the proceeds from this offering, we have and reserve broad discretion in the application of these proceeds. Accordingly, we reserve the right to use these proceeds for different purposes or uses which we have not listed above. The amounts and timing of our actual expenditures for each purpose may vary significantly depending upon numerous factors, including the status of our product development efforts, regulatory approvals, competition, marketing and sales activities and the market acceptance of any products introduced by us. Should we determine to employ cash resources for the acquisition of complementary businesses, products, or technologies, the amounts available for the purposes cited above may be significantly reduced.

Until we use the net proceeds of this offering for the above purposes, we intend to invest the net proceeds of this offering in short-term, investment grade, interest-bearing securities.

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Capitalization

The following table sets forth our cash and cash equivalents and capitalization as of September 30, 2004:

- on an actual basis; and
- on an adjusted basis to give effect to the sale of 7,000,000 shares of our common stock we are offering, after deducting underwriting discounts and commissions and estimated offering expenses to be paid by us.

	As of September 30, 2004	
	Actual	As adjusted
(In thousands, except per share amounts)	(unaudited)	
Cash and cash equivalents	$ 55,016	$ 80,836
Total debt and capital lease obligations	$ 17,725	$ 17,725
Stockholders equity:		
Preferred stock, par value $0.01 per share; 5,000 shares authorized; none outstanding		
Common stock, par value $0.01 per share; 50,000 shares authorized; 24,717 shares issued and outstanding, actual; 31,717 shares issued and outstanding, as adjusted	247	317
Additional paid-in capital	248,027	273,777
Deferred compensation	(53)	(53)
Deficit accumulated during the development stage	(176,392)	(176,392)
Total stockholders equity	$ 71,829	$ 97,649

The table above should be read in conjunction with our financial statements and related notes incorporated by reference in this prospectus supplement. This table excludes:

- 5,166,254 shares of our common stock issuable upon exercise of options outstanding as of September 30, 2004, at a weighted average exercise price of $16.89 per share, of which options to purchase 2,754,285 shares were exercisable as of that date at a weighted average exercise price of $18.67 per share;
- 1,392,019 shares of our common stock available for future grant under our 2004 Equity Incentive Plan as of September 30, 2004; and
- 1,050,000 shares of our common stock that may be purchased by the underwriters to cover over- allotments, if any.

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Market price of common stock

Our common stock is traded publicly through The NASDAQ National Market under the symbol NTEC. The following table presents quarterly information on the price range of our common stock. This information indicates the high and low sales prices reported by The NASDAQ National Market. These prices do not include retail markups, markdowns or commissions.

	High	Low
Year ended December 31, 2003		
First quarter	$ 9.31	$6.03
Second quarter	12.64	6.88
Third quarter	11.06	8.50
Fourth quarter	9.83	7.20
Year ended December 31, 2004		
First quarter	$13.80	$8.73
Second quarter	10.62	6.50
Third quarter	8.78	6.45
Fourth quarter	8.19	6.10
Year ending December 31, 2005		
First quarter (through February 17, 2005)	$ 7.25	$4.76

As of December 31, 2004, there were approximately 176 holders of record of our common stock. On February 17, 2005, the last sale price reported on The NASDAQ National Market for our common stock was $4.76 per share.

Dividend policy

We have never declared or paid any cash dividends on our common stock. We currently intend to retain all of our future earnings, if any, to finance operations, and we do not anticipate paying cash dividends 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.

Dilution

If you invest in our common stock, you will experience dilution to the extent of the difference between the public offering price per share you pay in this offering and the net tangible book value per share of our common stock immediately after this offering. Our net tangible book value as of September 30, 2004 was approximately $70.0 million, or $2.83 per share of common stock. Net tangible book value per share is equal to our total tangible assets minus total liabilities, all divided by the number of shares of common stock outstanding as of September 30, 2004. After giving effect to the sale of the 7,000,000 shares of common stock we are offering, and after deducting underwriting discounts and commissions and our estimated offering expenses, our as adjusted net tangible book value would have been approximately $95.8 million, or approximately $3.02 per share of common stock. This represents an immediate increase in net tangible book value of approximately $0.19 per share to existing

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stockholders and an immediate dilution of approximately $0.98 per share to new investors. The following table illustrates this calculation on a per share basis:

Public offering price per share		$4.00
Net tangible book value per share as of September 30, 2004	$2.83	
Increase per share attributable to the offering	0.19	
As adjusted net tangible book value per share after this offering		3.02
Dilution per share to new investors		$0.98

If the underwriters exercise their over-allotment option in full, as adjusted net tangible book value would increase to approximately $3.04 per share, representing an increase to existing stockholders of approximately $0.21 per share, and there would be an immediate dilution of approximately $0.96 per share to new investors.

The number of shares of common stock outstanding used for existing stockholders in the table and calculations above is based on shares outstanding as of September 30, 2004 and excludes:

- 5,166,254 shares of our common stock issuable upon exercise of options outstanding as of September 30, 2004, at a weighted average exercise price of $16.89 per share, of which options to purchase 2,754,285 shares were exercisable as of that date at a weighted average exercise price of $18.67 per share; and

- 1,392,019 shares of our common stock available for future grant under our 2004 Equity Incentive Plan as of September 30, 2004.

The exercise of outstanding options having an exercise price less than the public offering price will increase dilution to new investors.

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Management

Set forth below is the name, age, position and a brief account of the business experience of each of our executive officers:

Name of executive officer	Age	Position
C. Boyd Clarke	56	President, Chief Executive Officer and Chairman
George J. Vergis, Ph.D.	43	Executive Vice President, Commercial and Clinical Development
Joseph J. Villafranca, Ph.D.	60	Executive Vice President, Pharmaceutical Development and Operations
David A. Zopf, M.D.	62	Executive Vice President and Chief Scientific Officer
A. Brian Davis	38	Senior Vice President and Chief Financial Officer
Debra J. Poul, Esq.	52	Senior Vice President, General Counsel and Secretary

C. Boyd Clarke, 56, has served on our Board, and as President and Chief Executive Officer, since March 2002, and became Chairman of our Board in May 2003. From December 1999 through March 2002, Mr. Clarke was President and Chief Executive Officer of Aviron, a biotechnology company developing vaccines, which was acquired by MedImmune, and was also Chairman from January 2001 through March 2002. From 1998 through 1999, Mr. Clarke was Chief Executive Officer and President of U.S. Bioscience, Inc., a biotechnology company focused on products to treat cancer, which also was acquired by MedImmune. Mr. Clarke served as President and Chief Operating Officer of U.S. Bioscience, Inc. from 1996 to 1998. From 1977 to 1996, Mr. Clarke held a number of positions at Merck & Co., Inc., including being the first President of Pasteur-Merieux MSD, and most recently as Vice President of Merck Vaccines. Mr. Clarke serves as a director of QLT Inc., a global pharmaceutical company, Rib-X Pharmaceuticals, Inc., a privately held biotechnology company, the Biotechnology Industry Organization and Pennsylvania BIO. Mr. Clarke has a B.S. in biochemistry, and an M.A. in history from the University of Calgary. Mr. Clarke also serves on the Board of Trustees to the Textile Museum in Washington, D.C.

George J. Vergis, Ph.D., 43, has served as our Executive Vice President, Commercial and Clinical Development since February 2004, after serving as our Senior Vice President, Business and Commercial Development since December 2002. From July 2001 to December 2002, he served as our Vice President, Business and Commercial Development. From January 1996 to May 2001, Dr. Vergis served as Vice President, New Product Development and Commercialization at Knoll Pharmaceutical Company, a division of BASF Pharma, responsible for the commercial planning, product development, and marketing for the immunology franchise. Prior to this position, Dr. Vergis was responsible for managing the endocrine business for BASF Pharma s Knoll Pharmaceutical Division. Dr. Vergis has held a variety of clinical and medical marketing positions at Wyeth Pharmaceuticals and Warner-Lambert Parke-Davis. Dr. Vergis received his BA in biology and history from Princeton University, his Ph.D. in physiology from The Pennsylvania State University, and his M.B.A. from Columbia University.

Joseph J. Villafranca, Ph.D., 60, has served as our Executive Vice President, Pharmaceutical Development and Operations since February 2004, after serving as our Senior Vice President, Pharmaceutical Development and Operations since October 2002. From 1992 to 2002, Dr. Villafranca held various positions at Bristol-Myers Squibb, serving most recently as Vice President of Biologics Strategy and Biopharmaceuticals Operations. Prior to Bristol-Myers, Dr. Villafranca spent 20 years at The Pennsylvania State University, including eight years as the Evan Pugh Professor of Chemistry. Dr. Villafranca earned a B.S. in chemistry from the State University of New York and a Ph.D. in biochemistry/chemistry from Purdue University. He completed his post-doctoral training in biophysics at the Institute for Cancer Research in Philadelphia.

David A. Zopf, M.D., 62, has served as our Executive Vice President since January 2002 and became Executive Vice President and Chief Scientific Officer in February 2004. He served as our Vice

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President, Drug Development from 1992 to January 2002. From 1991 to 1992, Dr. Zopf served as a consultant to Neose. From 1988 to 1991, Dr. Zopf served as Vice President and Chief Operating Officer of BioCarb, Inc., a biotechnology company and the U.S. subsidiary of BioCarb AB, where he managed the research and development programs of novel carbohydrate-based diagnostics and therapeutics. Dr. Zopf received his A.B. in zoology from Washington University, and his M.D. from Washington University School of Medicine.

A. Brian Davis, 38, has served as our Senior Vice President and Chief Financial Officer since January 2005. From August 2002 until January 6, 2005, he served as our Vice President, Finance, and from 1994 until August 2002, Mr. Davis served in a variety of positions, most recently as Acting Chief Financial Officer and Senior Director, Finance. From 1991 to 1994, Mr. Davis was employed by MICRO HealthSystems, Inc., a provider of healthcare information systems, where he served most recently as Corporate Controller. Mr. Davis is licensed as a Certified Public Accountant, received his B.S. in accounting from Trenton State College and his M.B.A. from the Wharton School of the University of Pennsylvania.

Debra J. Poul, Esq., 52, has served as our Senior Vice President, General Counsel and Secretary since December 2002. From May 2002 to December 2002, she served as our Vice President, General Counsel and Secretary and from January 2000 until May 2002, she served as our General Counsel and Secretary. From January 1995 to January 2000, Ms. Poul was Of Counsel at Morgan, Lewis & Bockius LLP. From September 1978 to December 1994, Ms. Poul was at Dechert Price & Rhoads LLP, serving as Counsel from 1989 to 1994. Ms. Poul received her B.A. from the University of Pennsylvania and her J.D. from Villanova University.

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Underwriting

We are offering the shares of our common stock described in this prospectus supplement through the underwriters named below. UBS Securities LLC, J.P. Morgan Securities Inc. and Jefferies & Company, Inc. are the representatives of the underwriters. UBS Securities LLC is the sole book-running manager of this offering. We have entered into an underwriting agreement with the representatives. Subject to the terms and conditions of the underwriting agreement, each of the underwriters has severally agreed to purchase the number of shares of common stock listed next to its name in the following table.

Underwriters	Number of shares
UBS Securities LLC	3,150,000
J.P. Morgan Securities Inc.	2,450,000
Jefferies & Company, Inc.	1,400,000
Total	7,000,000

The underwriting agreement provides that the underwriters must buy all of the shares if they buy any of them. However, the underwriters are not required to take or pay for the shares covered by the underwriters over-allotment option described below.

Our common stock is offered subject to a number of conditions, including:

- receipt and acceptance of our common stock by the underwriters, and
- the underwriters right to reject orders in whole or in part.

In connection with this offering, certain of the underwriters or securities dealers may distribute prospectuses electronically.

OVER-ALLOTMENT OPTION

We have granted the underwriters an option to buy up to an aggregate of 1,050,000 additional shares of our common stock. The underwriters may exercise this option solely for the purpose of covering over-allotments, if any, made in connection with this offering. The underwriters have 30 days from the date of this prospectus supplement to exercise this option. If the underwriters exercise this option, they will each purchase additional shares approximately in proportion to the amounts specified in the table above.

COMMISSIONS AND DISCOUNTS

Shares sold by the underwriters to the public will initially be offered at the offering price set forth on the cover of this prospectus supplement. Any shares sold by the underwriters to securities dealers may be sold at a discount of up to $0.14 per share from the public offering price. Any of these securities dealers may resell any shares purchased from the underwriters to other brokers or dealers at a discount of up to $0.10 per share from the public offering price. If all the shares are not sold at the public offering price, the representatives may change the offering price and the other selling terms.

The following table shows the per share and total underwriting discounts and commissions we will pay to the underwriters, assuming both no exercise and full exercise of the underwriters option to purchase up to an additional 1,050,000 shares:

	No exercise	Full exercise
Per share	$ 0.24	$ 0.24
Total	$ 1,680,000	$ 1,932,000

We estimate that the total expenses of this offering payable by us, not including the underwriting discounts and commissions, will be approximately $500,000.

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Underwriting

In compliance with NASD guidelines, the maximum commission or discount to be received by any NASD member or independent broker-dealer may not exceed 8% of the aggregate amount of the securities offered pursuant to this prospectus supplement.

NO SALES OF SIMILAR SECURITIES

We, our executive officers and substantially all of our directors have entered into lock-up agreements with the underwriters. Under these agreements, subject to certain exceptions, we and each of these persons may not, without the prior written approval of UBS Securities LLC, offer, sell, contract to sell or otherwise dispose of, directly or indirectly, or hedge our common stock or securities convertible into or exchangeable or exercisable for our common stock. These restrictions will be in effect for a period of 90 days after the date of this prospectus supplement. The 90-day lock-up period may be extended under certain circumstances where we announce or pre-announce earnings or material news or a material event within approximately 18 days prior to, or approximately 16 days after, the termination of the 90-day period. At any time and without public notice, UBS Securities LLC may in its sole discretion release all or some of the securities from these lock-up agreements.

INDEMNIFICATION AND CONTRIBUTION

We have agreed to indemnify the underwriters and their controlling persons against certain liabilities, including liabilities under the Securities Act. If we are unable to provide this indemnification, we will contribute to payments the underwriters and their controlling persons may be required to make in respect of those liabilities.

NASDAQ NATIONAL MARKET LISTING

Our common stock is listed on The NASDAQ National Market under the symbol NTEC.

PRICE STABILIZATION, SHORT POSITIONS, PASSIVE MARKET MAKING

In connection with this offering, the underwriters may engage in activities that stabilize, maintain or otherwise affect the price of our common stock, including:

- stabilizing transactions;
- short sales;
- purchases to cover positions created by short sales;
- imposition of penalty bids;
- syndicate covering transactions; and
- passive market making.

Stabilizing transactions consist of bids or purchases made for the purpose of preventing or retarding a decline in the market price of our common stock while this offering is in progress. These transactions may also include making short sales of our common stock, which involve the sale by the underwriters of a greater number of shares of common stock than they are required to purchase in this offering, and purchasing shares of common stock on the open market to cover positions created by short sales. Short sales may be covered short sales, which are short positions in an amount not greater than the underwriters over-allotment option referred to above, or may be naked short sales, which are short positions in excess of that amount.

The underwriters may close out any covered short position either by exercising their over-allotment option, in whole or in part, or by purchasing shares in the open market. In making this determination, the underwriters will consider, among other things, the price of shares available for purchase in the open market compared to the price at which they may purchase shares through the over-allotment option. Naked short sales are in excess of the over-allotment option. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more

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Underwriting

likely to be created if the underwriters are concerned that there may be downward pressure on the price of the common stock in the open market that could adversely affect investors who purchased in this offering.

The underwriters also may impose a penalty bid. This occurs when a particular underwriter repays to the underwriters a portion of the underwriting discount received by it because the representatives have repurchased shares sold by or for the account of that underwriter in stabilizing or short covering transactions.

As a result of these activities, the price of our common stock may be higher than the price that otherwise might exist in the open market. If these activities are commenced, they may be discontinued by the underwriters at any time. The underwriters may carry out these transactions on The NASDAQ National Market, in the over-the-counter market or otherwise.

In addition, in connection with this offering certain of the underwriters (and selling group members) may engage in passive market making transactions in our common stock on The NASDAQ National Market prior to the pricing and completion of this offering. Passive market making consists of displaying bids on The NASDAQ National Market no higher than the bid prices of independent market makers and making purchases at prices no higher than these independent bids and effected in response to order flow. Net purchases by a passive market maker on each day are generally limited to a specified percentage of the passive market maker s average daily trading volume in the common stock during a specified period and must be discontinued when such limit is reached. Passive market making may cause the price of our common stock to be higher than the price that otherwise would exist in the open market in the absence of these transactions. If passive market making is commenced, it may be discontinued at any time.

AFFILIATIONS

The underwriters and their affiliates have provided and may provide certain commercial banking, financial advisory and investment banking services for us for which they receive fees.

The underwriters and their affiliates may from time to time in the future engage in transactions with us and perform services for us in the ordinary course of their business.

UBS Securities LLC has agreed to reimburse us certain amounts that it was paid previously, in its capacity as placement agent, as a result of the sale of shares of our common stock to certain of our management members and an entity affiliated with one of our directors in a May 2004 offering.

Legal matters

The validity of the shares of common stock we are offering will be passed upon for us by Pepper Hamilton LLP, Philadelphia, Pennsylvania. Certain legal matters in connection with this offering will be passed upon for the underwriters by Willkie Farr & Gallagher LLP, New York, New York.

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PROSPECTUS

$75,000,000

Neose Technologies, Inc.

Common Stock

We may sell from time to time shares of common stock in one or more offerings and the total offering price, in the aggregate, will not exceed $75,000,000. This means:

- we will provide a prospectus supplement each time we issue common stock; and
- the prospectus supplement will inform you about the specific terms of that offering and may also add, update or modify information contained in this document.

Our common stock is listed on The Nasdaq National Market under the symbol NTEC. On January 5, 2005, the reported last sale price of our common stock on The Nasdaq National Market was $6.25 per share.

Our principal offices are located at 102 Witmer Road, Horsham, Pennsylvania 19044, and our telephone number is (215) 315-9000.

Investing in our common stock involves risks. You should carefully consider the Risk Factors beginning on page 1 of this Prospectus before you decide to invest.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus. Any representation to the contrary is a criminal offense.

The date of this Prospectus is January 10, 2005.

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You should rely only on the information contained in this prospectus. We have not authorized anyone to provide you with information different from that contained or incorporated by reference in this prospectus. We may from time to time offer to sell, and seek offers to buy, our common stock in jurisdictions where offers and sales are permitted. The information contained in this prospectus may only be accurate as of the date of this prospectus.

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Who we are

We are a biopharmaceutical company using our enzymatic technologies to develop novel and improved therapeutics, focusing primarily on therapeutic proteins. Most therapeutic proteins on the market today are glycoproteins, which consist of a protein backbone (comprised of amino acids) to which carbohydrate structures (chains of simple sugars) are attached. While the protein backbone determines what the protein will do, the attached carbohydrate structures are often essential to ensure its proper functioning. We use our enzymatic technologies to build out carbohydrate structures on proteins and to attach compounds, such as polyethylene glycol, that could improve the drug properties of the modified protein. We are using these technologies to develop improved versions of drugs with proven efficacy and to improve the therapeutic profiles of glycoproteins being developed by our partners. We expect these modified proteins to offer significant advantages over the original versions of the drugs that are now on the market, including less frequent dosing and improved safety and efficacy. While our current focus is protein drug development, we are exploring opportunities to use our enzymatic technologies to construct other therapeutics, such as glycopeptides and glycolipids.

We were incorporated in Delaware in May 1991. Our executive offices are located at 102 Witmer Road, Horsham, PA 19044, our telephone number is 215-315-9000 and our website is at *http://www.neose.com*. Information contained on our website is not incorporated into this registration statement.

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Risk factors

You should carefully consider the risks described below before making an investment decision. These are the material risks currently known to us. Additional risks not presently known to us or that we currently deem immaterial may also impair our business operations.

Our business, financial condition or results of operations could be materially adversely affected by any of these risks. The trading price of our common stock could decline due to any of these risks, and you may lose all or part of your investment.

This prospectus also contains forward-looking statements that involve risks and uncertainties. Our actual results could differ materially from those anticipated in these forward-looking statements as a result of certain factors, including the risks faced by us described below and elsewhere in this prospectus.

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 our existing collaborations and license arrangements, and interest income should be sufficient to meet our operating and capital requirements through 2005, 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:

- the level of research and development investment required to develop our therapeutic proteins, and maintain and improve our technology position;
- the costs of obtaining or manufacturing 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 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; and
- our need or decision to acquire or license complementary technologies or new drug targets.

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Risk factors

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

If we raise additional capital by issuing equity securities, our existing stockholders percentage ownership will be reduced and they may experience substantial dilution. We may also issue equity securities that provide for rights, preferences, 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 entered into a credit agreement with a bank, dated as of January 30, 2004, on which the balance, as of September 30, 2004, was $9.0 million. Under the credit agreement, 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 September 30, 2004, our total outstanding debt was $17.7 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.

Under our credit agreement, 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 credit agreement. Under the credit agreement, if we fail at any time to maintain a minimum required cash and short-term investments balance of at least $22.0 million, or at any time after January 30, 2008, the bank has 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, which may have the effect of requiring us to repay the then outstanding loan balance under the credit agreement. As of September 30, 2004, we maintained a cash balance of $55.0 million.

The credit agreement also contains 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 credit agreement could result in a default under our credit agreement. Upon the occurrence of such an event of default, the bank could elect to declare all amounts outstanding thereunder 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, including net losses of $13.3 million for the year ended December 31, 2001, $26.4 million for the year ended December 31, 2002, $37.7 million for the year ended December 31, 2003, and $30.7 million for the nine months ended September 30, 2004. Given our planned level of operating expenses, we expect to continue incurring losses for some time. As of September 30, 2004, we had an accumulated deficit of approximately $176.4 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

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these sources and from the licensing of our technologies. We also expect to spend significant amounts to expand our research and development on our proprietary drug candidates and technologies, maintain and expand our intellectual property position, expand our manufacturing scale-up activities, and expand our business development and commercialization efforts. 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 developed any products or commercialized any products or technologies, and we may never be able to do so. Since we began operations in 1990, we have not generated any revenues, except 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
- 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 remodeling 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 one marketed erythropoietin (EPO) product was associated with pure red cell aplasia in post-marketing surveillance studies. This highlights the fact that even after a product is approved for marketing, problems may arise which can negatively affect sales and increase costs.

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.

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Risk factors

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 proteins or the enzymes, sugar nucleotides, and other reagents we use to modify proteins. We 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 the EPO protein that we are currently manufacturing to support preclinical and early clinical development of our remodeled EPO candidate. Our success with this program will depend on our ability to manufacture this protein, at commercial scale, in the baculovirus/insect cell expression system (the production source of our EPO protein), either independently or with a collaborator or supplier. To date, no product produced in this expression system has received marketing authorization in the U.S. or European Union, which means that we may face previously unidentified problems resulting from the use of this expression system and related regulatory challenges.

We are also manufacturing, directly or through suppliers, the enzymes, sugar nucleotides and other reagents we need to apply our technologies. We have sought and continue to seek collaborators, licensees, or contract manufacturers to manufacture at least some of the compounds necessary to commercialize our technologies. We may not be able to find parties willing and able to manufacture these compounds at acceptable prices, 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 manufacture these compounds on a commercial scale or to obtain commercial quantities, in either case, at reasonable cost. Our manufacturing processes also must comply with current Good Manufacturing Practices, or cGMP, prescribed by the U.S. Food and Drug Administration, or FDA. We may not be able to manufacture or obtain sufficient quantities of the products we develop to meet our needs for pre-clinical or clinical development, and we may have problems complying, or maintaining compliance, with cGMP.

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

If we encounter delays or difficulties in connection with manufacturing, commercialization of our products and technologies could be delayed, and we could breach our obligations under our collaborative agreements and we may 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 A/ S and BioGeneriX AG. 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 adapting our technologies to the needs of our collaborative partners;
- our collaborators may not be successful in, or may not remain committed to, co-developing our products or commercializing products incorporating our technologies;
- our collaborators may not commit sufficient resources to incorporating our technologies into their products;
- our collaborators may seek to develop other proprietary alternatives to our products or technologies;

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- 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.

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

We may be exposed to product liability and related risks.

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

RISKS RELATED TO INTELLECTUAL PROPERTY

Blocking patents or claims of infringement may stop or delay or 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. As we seek to develop next-generation proprietary products, we devote significant resources to investigate the patent protection surrounding our target proteins. Patent protection for therapeutic proteins often comprises numerous claims for composition of matter, methods of use, and methods of making. The numerous patents 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. In addition, we rely on certain exemptions in order to conduct the necessary research and development to support our regulatory filings. Our interpretation of patents or reliance on exemptions 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 an improved 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. 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.

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

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

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

- the pending patent applications we have filed or to which we have exclusive rights may not result in issued patents or may take longer than we expect to result in issued patents;
- we may be subject to interference proceedings;
- we may be subject to opposition proceedings in foreign countries;
- the claims of any patents that are issued may not provide meaningful protection;
- we may not be able to develop additional proprietary technologies that are patentable;
- the patents licensed or issued to us or our customers may not provide a competitive advantage;
- other companies may challenge patents licensed or issued to us or our customers;
- other companies may independently develop similar or alternative technologies, or duplicate our technologies;
- other companies may design around technologies we have licensed or developed; and
- enforcement of patents is complex, uncertain and expensive.

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.

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

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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.

International patent protection is uncertain.

In addition to the issues discussed under the previous risk, patent law outside the U.S. differs from country to country. The laws of some foreign countries may not protect our intellectual property rights to the same extent as U.S. laws. We may participate in opposition proceedings to determine the validity of foreign patents belonging to us or our competitors, which proceedings could result in substantial costs and diversion of our efforts. Finally, some of our patent protection in the U.S. is not available to us in foreign countries due to the differences in the patent laws of those countries.

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

We have licensed patents and patent applications from a number of institutions. Some of our proprietary rights have been licensed to us under agreements that have performance requirements or other contingencies. The failure to comply with these provisions could lead to termination or modifications of our rights to these licenses. Additionally, we may need to obtain additional licenses to patents or other proprietary rights from other parties to facilitate development of our proprietary technology base. 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, Enzon, Human Genome Sciences, BioRexis and Alkermes. Other companies have programs focused on developing next-generation or improved versions of EPO and granulocyte colony stimulating factor (G-CSF), and some are already marketing improved versions of these products. These companies include Amgen, Roche, Transkaryotic Therapeutics, Human Genome Sciences, Maxygen, ARIAD and Affymax. 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. These companies include Crucell, GLYCART, GlycoFi and Momenta.

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.

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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 remodeling our target proteins or the target proteins of our potential collaborators.

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

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

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

Because of the specialized scientific nature of our business, we are highly dependent upon qualified scientific, technical and managerial personnel, including our research and development team and our president and CEO, C. Boyd Clarke. The advancement of our business is dependent upon our management team s ability to evaluate collaboration opportunities and on our CEO s ability to focus the Company s efforts. Our anticipated research and development efforts will require additional expertise and the addition of new qualified personnel. There is intense competition for qualified management and research and development personnel in the pharmaceutical field. Therefore, we may not be able to attract and retain the qualified personnel necessary for 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, would harm our research and development programs, our ability to manage day-to-day operations, attract collaboration partners, attract and retain other employees, and generate revenues. We do not maintain key man life insurance on any of our employees.

RISKS RELATED TO GOVERNMENT REGULATION

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

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

Pharmaceutical product candidates manufactured using our technologies must undergo an extensive regulatory approval process before commercialization. This process is regulated by the FDA and by comparable agencies in the European Union 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.

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 baculovirus/insect cell expression system. To our knowledge, no compound for human use produced in this expression system has been submitted for

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marketing authorization in the U.S. or EU, and we may encounter delays 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 would be subject to continued review by the FDA and other regulatory authorities. Any later discovery of unknown problems with our products, products incorporating our technologies, or manufacturing processes could result in restrictions on such products or manufacturing processes, including potential withdrawal of the products from the market. In addition, if regulatory authorities determine that we 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.

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RISKS RELATED TO FACILITIES, BUSINESS INTERRUPTION, AND THE ENVIRONMENT

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

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

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

Activists and terrorists have shown a willingness to injure people and damage physical facilities, equipment and biological materials to publicize or otherwise further their ideological causes. Our 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.

RISKS RELATED TO STOCK MARKET

Our stock price may continue to experience fluctuations.

The market prices of securities of thinly-traded biotechnology companies, such as ours, generally are highly volatile. For example, in the past 24 months, the price of our common stock reached a low of $6.03 per share in February 2003 and a high of $13.80 per share in January 2004. During the past 12 months the price of our common stock has traded as low as $6.10 per share in December 2004 and as high as $13.80 per share in January 2004.

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

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

- preclinical and clinical trial results;
- product development delays;
- an announcement or termination of a collaborative relationship by us or any of our partners or competitors;
- developments relating to our patent position or other proprietary rights;
- announcements of technological innovations or new therapeutic products;

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- 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, or if any unforeseen risk affected our performance, it could have a dramatic and adverse impact on the market price of our common stock.

FOREIGN EXCHANGE RISKS

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

We have entered into 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 value 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.

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About this prospectus

This prospectus is part of a shelf registration statement that we filed with the Securities and Exchange Commission (the SEC). By using a shelf registration statement, we may sell, from time to time, in one or more offerings, shares of common stock in a dollar amount that does not exceed $75,000,000. For further information about our business, and the securities, you should refer to the registration statement, the reports incorporated by reference in this prospectus, and its exhibits. The exhibits to our registration statement contain the full text of certain contracts and other important documents we have summarized in this prospectus. Since these summaries may not contain all the information that you may find important in deciding whether to purchase the securities we may offer, you should review the full text of these documents. The registration statement can be obtained from the SEC as indicated under the heading Where You Can Find More Information.

You should rely only on the information contained or incorporated by reference in this prospectus and in the applicable prospectus supplement. We have not authorized anyone to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. We will not make an offer to sell our common stock in any jurisdiction where the offer or sale is not permitted. You should assume that the information appearing in this prospectus, as well as information we previously filed with the SEC and incorporated by reference in this prospectus, is accurate only as of the date on the front cover of this prospectus. Our business, financial condition, results of operations and prospects may have changed since that date.

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Special note regarding forward-looking statements

Some of the statements in the sections entitled Who We Are and Risk Factors and elsewhere in this prospectus, including the documents incorporated herein by reference, contain forward-looking statements within the meaning of Section 27A of the Securities Act. When used in this prospectus and the documents incorporated herein by reference, the words anticipate, believe, estimate, may, expect, intend, should will, predict, potential, continue, the negative of such terms and similar expressions are generally intended to identify forward-looking statements. These forward-looking statements include, among others, the statements about our:

- estimate of the length of time that our existing cash, cash equivalents and any marketable securities, expected revenue, and interest income will be adequate to finance our operating and capital requirements;
- 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, manufacture commercial quantities of reagents and products, and commercialize our technology;
- expectations for the development of an improved EPO, G-CSF, and subsequent proprietary drug candidates;
- expectations for incurring additional capital expenditures for renovations of our facilities;
- 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.

Our actual results could differ materially from the results expressed in, or implied by, these 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 project timelines;
- 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;
- 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 and our collaborators ability to develop and commercialize therapeutic proteins and our ability to commercialize our technologies;
- our ability to compete successfully in an intensely competitive field;

- our ability to renovate our facilities as required for our operations;
- our ability to attract and retain key personnel; and

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Special note regarding forward-looking statements

4 general economic conditions

These and other risks and uncertainties that could affect our actual results are discussed in this prospectus, particularly in the section entitled RISK FACTORS, and in our other filings with the SEC.

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 prospectus to conform them to actual results, except as required by the federal securities laws.

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Use of proceeds

Except as otherwise described in the applicable prospectus supplement, the net proceeds from the sale of our common stock offered hereunder will be added to our general funds and used for general corporate purposes, which may include, but are not limited to:

- ongoing research and development activities, and the conduct of human clinical trials, for our proprietary protein product candidates;
- capital expenditures;
- expansion, through the lease or purchase of additional facilities, or remodeling and development of portions of our existing facilities, as required for our research and development activities, manufacturing operations and corporate staff;
- debt retirement;
- potential acquisitions; and
- general working capital.

The amounts and timing of our actual expenditures for each purpose may vary significantly depending upon numerous factors, including the status of our product development efforts, regulatory approvals, competition, and funding by collaborators. Pending such uses, we intend to invest the net proceeds of this offering in short-term, investment grade, interest-bearing securities.

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Description of capital stock

Under our certificate of incorporation our authorized capital stock consists of 50,000,000 shares of common stock, par value $0.01 per share, and 5,000,000 shares of preferred stock, par value $0.01 per share. As of January 6, 2005 , we had 24,717,171 shares of common stock outstanding and no shares of preferred stock outstanding. As of January 6, 2005, we had reserved for issuance 300,000 shares of series A junior participating preferred stock in connection with our stockholder rights agreement described below. As of the date of this prospectus, we have not issued any shares of our series A junior participating preferred stock.

COMMON STOCK

Voting. For all matters submitted to a vote of stockholders, each holder of common stock is entitled to one vote for each share registered in his, her or its name. Our common stock does not have cumulative voting rights. As a result, subject to the voting rights of any outstanding preferred stock, of which there currently is none, persons or a group of persons who hold more than 50% of the outstanding common stock entitled to elect members of our board of directors can elect all of the directors who are up for election in a particular year.

Dividends. If our board of directors declares a dividend, holders of common stock would receive payments from our funds that are legally available to pay dividends. However, this dividend right would be subject to any preferential dividend rights we may grant to holders of preferred stock, if any is outstanding.

Liquidation and Dissolution. If we liquidate or dissolve, the holders of our common stock would be entitled to share ratably in all the assets that remain after we pay our liabilities and any preferential liquidation or dissolution rights we may owe to holders of preferred stock, if any is outstanding.

Other Rights and Restrictions. Holders of our common stock do not have preemptive rights, and they have no right to convert their common stock into any other securities. Our common stock is not subject to redemption by us. The rights, preferences and privileges of holders of our common stock are subject to the rights of the holders of any series of preferred stock which we may designate in the future. Our certificate of incorporation and bylaws do not restrict the ability of a holder of common stock to transfer his, her or its shares of common stock. When we issue shares of common stock under this prospectus, the shares will be fully paid and non-assessable and will not have, or be subject to, any preemptive or similar rights.

Listing. Our common stock is listed on The Nasdaq National Market under the symbol NTEC .

Transfer Agent and Registrar. The transfer agent and registrar for our common stock is American Stock Transfer & Trust Company, 40 Wall Street, New York, New York 10005.

PREFERRED STOCK

Our certificate of incorporation authorizes the issuance of up to 5,000,000 shares of preferred stock, par value $0.01 per share. We have reserved for issuance 300,000 shares of series A junior participating preferred stock in connection with our stockholder rights agreement. We may issue, from time to time in one or more series, up to 4,700,000 shares of preferred stock, the terms of which may be determined at the time of issuance by our board of directors, without further action by our stockholders, and may include voting rights, including the right to vote as a series on particular matters, preferences as to dividends and liquidation, conversion rights, redemption rights and sinking fund provisions.

CERTAIN EFFECTS OF AUTHORIZED BUT UNISSUED STOCK

We have shares of our common stock and preferred stock available for future issuance without stockholder approval. We may utilize these additional shares for a variety of corporate purposes,

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including future public offerings to raise additional capital, facilitating corporate acquisitions or paying a dividend on the capital stock.

The existence of unissued and unreserved common stock and preferred stock may enable our board of directors to issue shares to persons friendly to current management or to issue preferred stock with terms that could render more difficult or discourage a third party attempt to obtain control of us by means of a merger, tender offer, proxy contest or otherwise, thereby protecting the continuity of our management. In addition, if we issue preferred stock, the issuance could adversely affect the voting power of holders of common stock and the likelihood that such holders will receive dividend payments and payments upon liquidation. The issuance of any preferred stock could adversely affect the rights of the holders of common stock and, therefore, reduce the value of the common stock.

We believe that the preferred stock provides us with increased flexibility in structuring possible future financings and acquisitions, and in meeting other corporate needs that might arise. Having such authorized shares available for issuance allows us to issue shares of preferred stock without the expense and delay of holding a special stockholders meeting. The authorized shares of preferred stock, as well as shares of common stock, will be available for issuance without further action by our stockholders, unless such action is required by applicable law or the rules of any stock exchange or quotation system on which our securities may be listed or quoted.

DELAWARE ANTI-TAKEOVER LAW

We are subject to Section 203 of the DGCL which, subject to certain exceptions and limitations, prohibits a Delaware corporation from engaging in any business combination with any interested stockholder for a period of three years following the date that such stockholder became an interested stockholder, unless:

(i) prior to such date, the board of directors of the corporation approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder;

(ii) upon consummation of the transaction which resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced (for the purposes of determining the number of shares outstanding under the DGCL, those shares owned (x) by persons who are directors and also officers and (y) by employee stock plans in which employee participants do not have the right to determine confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer are excluded from the calculation); or

(iii) on or subsequent to such date, the business combination is approved by the board of directors and authorized at an annual or special meeting of stockholders, and not by written consent, by the affirmative vote of at least 66 2/3% of the outstanding voting stock which is not owned by the interested stockholder.

For purposes of Section 203, a business combination includes:

(i) any merger or consolidation involving the corporation and the interested stockholder;

(ii) any sale, transfer, pledge or other disposition of 10% or more of either the aggregate market value of all of the assets of the corporation determined on a consolidated basis or the aggregate market value of all of the outstanding stock of the corporation involving the interested stockholder;

(iii) subject to certain exceptions, any transaction which results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder;

(iv) any transaction involving the corporation which has the effect of increasing the proportionate share of the stock of any class or series of the corporation beneficially owned by the interested stockholder; or

(v) the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges or other financial benefits provided by or through the corporation.

For purposes of Section 203, an interested stockholder is defined as any entity or person beneficially owning 15% or more of the outstanding voting stock of the corporation and any entity or person affiliated with or controlling or controlled by such entity or person.

SELECTED CERTIFICATE OF INCORPORATION AND BYLAW PROVISIONS

Our certificate of incorporation and by-laws authorize our board of directors to fill vacant directorships or increase the size of our board without stockholder action. In addition, Delaware law and our by-laws provide that directors may only be removed by the stockholders by the affirmative vote of a majority of our outstanding securities then entitled to vote in the election of directors.

Our certificate of incorporation eliminates the ability of stockholders to act by written consent. Our by-laws provide that special meetings of stockholders may be called only by our president and shall be called by our president or secretary at the request in writing of a majority of our board of directors.

The preceding provisions could have the effect of discouraging, delaying or making more difficult certain attempts to acquire us or remove incumbent directors even if a majority of our stockholders believe the attempt to be in their or our best interests.

Our by-laws provide that stockholders seeking to bring business before an annual meeting of stockholders, or to nominate candidates for election as directors at the annual meeting of stockholders, must provide us with timely written notice of their proposal or nomination. To be timely, a stockholder s notice must be delivered to or mailed and received at our principal executive offices not less than 120 days before the one year anniversary of the date of the preceding year s proxy statement sent to stockholders in connection with the annual meeting of stockholders. Our by-laws also specify certain requirements as to the form and content of a stockholder s notice. These provisions may preclude stockholders from bringing matters before the annual meeting of stockholders or from making nominations for directors at an annual meeting of stockholders.

Delaware law provides generally that the affirmative vote of a majority of the shares entitled to vote on any matter is required to amend a corporation s certificate of incorporation or by-laws, unless a corporation s certificate of incorporation or by-laws, as the case may be, requires a greater percentage. Our by-laws require the affirmative vote of at least 75% of the votes that all stockholders would be entitled to cast at an annual election of directors in order to amend, repeal or adopt any by-law provision that is inconsistent with the current by-law provisions relating to the stockholders rights to nominate directors and propose business at an annual or special meeting of the stockholders. In addition, our board of directors is authorized to adopt, amend or repeal any provision of our by-laws without stockholder approval.

STOCKHOLDER RIGHTS PLAN

On September 17, 1997, our board of directors adopted a stockholder rights plan and, in connection with that plan, designated 300,000 shares of series A junior participating preferred stock. Under this plan, a preferred share purchase right was issued as a dividend on each outstanding share of our common stock as of October 6, 1997. This preferred share purchase right entitles its holder to purchase from us a unit consisting of 1/100th of a share of our series A junior participating preferred stock at an exercise price of $150 per unit, subject to adjustment. Each unit carries voting and dividend rights that are intended to produce the equivalent of one share of common stock. These rights expire on October 6, 2007.

The preferred share purchase rights granted under the stockholder rights plan generally will be exercisable and will trade separately from our common stock only if a person or group acquires beneficial ownership of 15% or more of our common stock. Only when one or more of these events occur will stockholders receive certificates for the rights granted under the stockholder rights plan. Except as discussed in the next paragraph, if any person actually acquires 15% or more of our

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common stock other than through a tender or exchange offer for our common stock at a price and on terms that provide fair value to all stockholders or if a holder of 15% or more of our common stock engages in certain self-dealing transactions or engages in a merger or other business combination in which we survive and our common stock remains outstanding, the other holders of our common stock will be able to exercise their preferred share purchase rights and receive shares of our common stock having a value equal to double the exercise price of the right. Additionally, if we are involved in certain other mergers where our shares are exchanged or certain major sales of our assets occur, the holders of our common stock will be able to exercise their preferred share purchase rights and receive shares of the acquiring company having a value equal to double the exercise price of the right. In either case, the holders of the rights may, in lieu of exercise, surrender the rights in exchange for one-half of the amount of securities otherwise purchasable. Upon the occurrence of any of these events, the preferred share purchase rights will no longer be exercisable for the purchase of series A junior participating preferred stock.

The original stockholder rights plan was amended and restated in 1998 and we have subsequently amended the stockholder rights plan to provide the following exceptions to the general provisions discussed above. We have agreed that Kopp Investment Advisors, Inc. (on its own behalf, or on behalf of LeRoy C. Kopp, Kopp Emerging Growth Fund, and Kopp Holding Company) will not trigger the share purchase rights until it (i) is the beneficial owner of 20% or more of our common stock or (ii) is the beneficial owner of 15% or more of our common stock and is not permitted to file a Schedule 13G, in lieu of a Schedule 13D, to report its beneficial ownership of our securities under the Securities Exchange Act of 1934, as amended, (the Exchange Act) and the rules and regulations promulgated thereunder. We have also agreed that Eastbourne Capital Management, LLC, and Richard Jon Barry, will not trigger the share purchase rights until they (i) are the beneficial owner of 25% or more of our common stock or (ii) are the beneficial owner of 15% or more of our common stock and are not permitted to file a Schedule 13G, in lieu of a Schedule 13D, to report their beneficial ownership of our securities under the Exchange Act, and the rules and regulations promulgated thereunder.

We will be entitled to redeem the preferred share purchase rights at $.01 per right at any time until the 10th day following a public announcement that a person has acquired a 15% ownership position in our common stock. In our discretion, we may extend the period during which we can redeem these rights.

STOCK OPTION PLAN

As of January 6, 2005, options to purchase a total of 5,113,824 shares of common stock have been granted and remain outstanding.

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Plan of distribution

We may sell the common stock being offered hereby at prices and under terms then prevailing, at prices related to the then current market price or in negotiated transactions from time to time in one or more of the following ways:

- through one or more underwriters on a firm commitment or best-efforts basis;
- through broker-dealers, who may act as agents or principals, including a block trade in which a broker or dealer so engaged will attempt to sell the shares as agent but may position and resell a portion of the block as principal to facilitate the transaction;
- directly to one or more purchasers;
- through agents;
- in privately negotiated transactions; and
- in any combination of these methods of sale.

We will set forth the terms of the offering of the common stock in a prospectus supplement, including:

- the name or names of any agents or underwriters, dealers or agents;
- the purchase price of the common stock being offered and the proceeds we will receive from the sale;
- any underwriting discounts and commissions or agency fees and other items constituting compensation to underwriters, dealers or agents;
- any over-allotment options under which underwriters may purchase additional securities from us;
- any discounts or concessions allowed or reallowed or paid to dealers; and
- any securities exchange on which the common stock may be listed.

The distribution of the common stock may be effected from time to time in one or more transactions at a fixed price or prices, which may be changed, at market prices prevailing at the time of sale, at prices related to the prevailing market prices or at negotiated prices.

UNDERWRITERS

If we use underwriters for a sale of common stock, the underwriters will acquire the common stock for their own account. Unless otherwise set forth in the applicable prospectus supplement, the underwriters may resell the common stock in one or more transactions, including negotiated transactions, at a fixed public offering price or at varying prices determined at the time of sale. The obligations of the underwriters to purchase the common stock will be subject to the conditions set forth in the applicable underwriting agreement. We may change from time to time any public offering price and any discounts or concessions the underwriters allow or reallow or pay to dealers. We may use underwriters with whom we have a material relationship. We will describe in the applicable prospectus supplement naming the underwriter the nature of any such relationship.

AGENTS

We may designate brokers, dealers and other agents who agree to use their reasonable efforts to solicit purchases for the period of their appointment or to sell common stock on a continuing basis. Brokers, dealers and other agents may receive compensation in the form of commissions, discounts or concessions from us. Brokers, dealers and other agents may also receive compensation from the purchasers of the common stock for whom they sell as principals. Each particular broker, dealer or other agent will receive compensation in amounts negotiated in connection with the sale, which might be in excess of customary commissions. We have not entered into any agreements, understandings or

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Plan of distribution

arrangements with any underwriters, brokers, dealers or other agents regarding the sale of common stock. As of the date of this prospectus, there are no special selling arrangements between any underwriter, broker, dealer, other agent or other person and us. No period of time has been fixed within which the common stock will be offered or sold.

If required under applicable state securities laws, we will sell the common stock only through registered or licensed brokers or dealers. In addition, in some states, we may not sell securities unless they have been registered or qualified for sale in the applicable state or an exemption from the registration or qualification requirement is available and complied with.

DIRECT SALES

We may also sell common stock directly to one or more purchasers without using underwriters, brokers, dealers or other agents. Brokers, dealers and other agents that participate in the distribution of the common stock may be underwriters as defined in the Securities Act and any discounts or commissions they receive from us and any profit on their resale of the common stock may be treated as underwriting discounts and commissions under the Securities Act. We will identify in the applicable prospectus supplement any underwriters, brokers, dealers or other agents and will describe their compensation. We may have agreements with the underwriters, brokers, dealers or other agents to indemnify them against specified civil liabilities, including liabilities under the Securities Act. Underwriters, brokers, dealers and other agents may engage in transactions with or perform services for us in the ordinary course of their businesses.

STABILIZATION ACTIVITIES

Any underwriter may engage in overallotment, stabilizing transactions, short covering transactions and penalty bids in accordance with Rule 104 of Regulation M under the Exchange Act. Overallotment involves sales in excess of the offering size, which create a short position. Stabilizing transactions permit bids to purchase the underlying security so long as the stabilizing bids do not exceed a specified maximum. Short covering transactions involve purchases of the common stock in the open market after the distribution is completed to cover short positions. Penalty bids permit the underwriters to reclaim a selling concession from a dealer when the common stock originally sold by the dealer are purchased in a covering transaction to cover short positions. Those activities may cause the price of the common stock to be higher than it would otherwise be. If commenced, the underwriters may discontinue any of the activities at any time. These transactions may be effected on The Nasdaq Stock Market or otherwise.

PASSIVE MARKET MARKING

Any underwriters who are qualified market markers on The Nasdaq National Market may engage in passive market making transactions in the common stock on The Nasdaq National Market in accordance with Rule 103 of Regulation M, during the business day prior to the pricing of the offering, before the commencement of offers or sales of the common stock. Passive market makers must comply with applicable volume and price limitations and must be identified as passive market makers. In general, a passive market maker must display its bid at a price not in excess of the highest independent bid for such security; if all independent bids are lowered below the passive market maker s bid, however, the passive market maker s bid must then be lowered when certain purchase limits are exceeded.

INDEMNIFICATION

Underwriters, brokers, dealers and other agents may be entitled under agreements entered into with us to indemnification by us against civil liabilities, including liabilities under the Securities Act, or to contribution by us to payments they may be required to make in respect thereof. The terms and conditions of the indemnification will be described in an applicable prospectus supplement.

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Plan of distribution

COSTS

We will bear all costs, expenses and fees in connection with the registration of the common stock, as well as the expense of all commissions and discounts, if any, attributable to the sales of the common stock by us.

ORDINARY COURSE RELATIONSHIPS

Underwriters, brokers, dealers and other agents may engage in transactions with, or be lenders to, us in the ordinary course of business.

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Legal matters

The validity of the shares of our common stock offered by this prospectus will be passed upon for us by Pepper Hamilton LLP, Philadelphia, Pennsylvania.

Experts

The financial statements of Neose Technologies, Inc. as of December 31, 2003 and 2002 and each of the years in the two-year period ended December 31, 2003, have been incorporated by reference herein and elsewhere in the registration statement on Form S-3 of which this prospectus forms a part, in reliance upon the report of KPMG LLP, independent accountants, incorporated by reference herein, and upon the authority of said firm as experts in accounting and auditing.

The financial statements incorporated by reference in this registration statement on Form S-3 of which this prospectus forms a part for the year ended December 31, 2001 and for the period from January 17, 1989 (inception) through December 31, 2003, to the extent related to the period from January 17, 1989 (inception) to December 31, 2001, have been incorporated by reference in reliance on the report of Arthur Andersen LLP, independent public accountants, given on the authority of said firm as experts in auditing and accounting.

Effective April 29, 2002, our board of directors approved the dismissal of Arthur Andersen LLP as our independent auditors and the appointment of KPMG LLP to serve as our independent auditors. After reasonable efforts, we have not been able to obtain the written consent of Arthur Andersen LLP to the incorporation by reference of its report into this Registration Statement. We have dispensed with the requirement to file the written consent of Arthur Andersen LLP in reliance on Rule 437a promulgated under the Securities Act. Since we have not been able to obtain the written consent of Arthur Andersen LLP, you will not be able to recover against Arthur Andersen LLP under Section 11 of the Securities Act for any untrue statements of material fact contained in the financial statements audited by Arthur Andersen LLP incorporated by reference herein or any omissions to state a material fact required to be stated therein.

Additional information

This prospectus is part of a registration statement we have filed with the SEC. This prospectus does not contain all of the information contained in the registration statement or the exhibits to the registration statement. For further information about us, please see the complete registration statement. Summaries of agreements or other documents in this prospectus are not necessarily complete. Please refer to the exhibits to the registration statement for complete copies of these documents.

We are subject to the information requirements of the Exchange Act and file reports, proxy statements and other information with the SEC. You may read and copy such reports, proxy statements and other information, including the registration statements and all of their exhibits, at the SEC public reference room at:

450 Fifth Street, N.W.

Judiciary Plaza
Room 1024
Washington, D.C. 20549

You may obtain information on the operation of the SEC public reference room in Washington, D.C. by calling the SEC at 1-800-SEC-0330. Our SEC filings, including the registration statement of which

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this prospectus forms a part and the documents incorporated by reference that are listed below, are also available from the SEC s Web site at *www.sec.gov*, which contains reports, proxy and information statements and other information regarding issuers that file electronically.

The SEC allows us to incorporate by reference into this prospectus certain information that we file with it. This means that we can disclose important information to you by referring you to another document that we filed separately with the SEC. The information incorporated by reference is deemed to be part of this prospectus, except for any information superseded by information in this prospectus. You should read the information incorporated by reference because it is an important part of this prospectus.

We incorporate by reference the following documents we have filed, or may file, with the SEC:

1. Our Annual Report on Form 10-K for the year ended December 31, 2003;

2. Our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2004, June 30, 2004 and September 30, 2004;

3. Our Current Reports on Form 8-K filed on April 20, 2004 (two reports filed on that date), April 26, 2004, May 14, 2004, May 19, 2004, May 21, 2004, September 24, 2004 and November 9, 2004;

4. The description of our common stock contained in the Registration Statement on Form 8-A filed with the SEC on February 7, 1996, as updated by the description included in our Current Report on Form 8-K filed with the SEC on May 14, 2004;

5. The description of rights to purchase preferred shares contained in the Registration Statement on Form 8-A filed with the SEC on October 1, 1997, as updated by the description included in our Current Report on Form 8-K filed with the SEC on May 14, 2004; and

6. All documents filed by us with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act after the date of the initial registration statement of which this prospectus is a part until the offering of shares pursuant to this prospectus is complete (other than those portions of such documents described in paragraphs (i), (k), and (l) of Item 402 of Regulation S-K promulgated by the SEC).

If you request, either orally or in writing, we will provide you with a copy of any or all documents which are incorporated by reference. We will provide such documents to you free of charge, but will not include any exhibits, unless those exhibits are incorporated by reference into the document. You should address written requests for documents to Debra J. Poul, Senior Vice President and General Counsel, Neose Technologies, Inc., 102 Witmer Road, Horsham, Pennsylvania 19044, (215) 315-9000.

We undertake no obligation to publicly update any forward-looking statements, whether as a result of new information, future events or otherwise. You are advised, however, to consult any further disclosures we make on related subjects in our 10-Q, 8-K and 10-K reports to the SEC. Also note that we provide a cautionary discussion of risks and uncertainties relevant to our business in the Risk Factors section of this prospectus. These are factors that we think could cause our actual results to differ materially from expected results. Other factors besides those listed here could also adversely affect us. This discussion is provided as permitted by the Private Securities Litigation Reform Act of 1995.

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