

NEOSE TECHNOLOGIES INC  
Form S-3  
December 09, 2004

As filed with the Securities and Exchange Commission on December 9, 2004

Registration No.333-

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# SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

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## FORM S-3

Registration Statement Under  
The Securities Act of 1933

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### Neose Technologies, Inc.

(Exact name of Registrant as specified in its charter)

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Delaware

13-3549286

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(State or other jurisdiction  
of incorporation or organization)

(I.R.S. Employer  
Identification No.)

102 Witmer Road  
Horsham, Pennsylvania 19044  
(215) 315-9000

(Address, including zip code, and telephone number, including area code, of Registrant's principal executive offices)

Debra J. Poul, Esquire  
Senior Vice President and General Counsel  
Neose Technologies, Inc.  
102 Witmer Road  
Horsham, Pennsylvania 19044  
(215) 315-9000

(Name, address, including zip code, and telephone  
number, including area code, of agent for service)

**COPY TO:**

Barry M. Abelson, Esquire  
Pepper Hamilton LLP  
3000 Two Logan Square  
Eighteenth and Arch Streets  
Philadelphia, PA 19103-2779  
(215) 981-4000

**Approximate date of commencement of proposed sale to the public:  
As soon as practicable after this Registration Statement becomes effective.**

If the only securities being registered on this Form are being offered pursuant to dividend or interest reinvestment plans, please check the following box:

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, other than securities offered only in connection with dividend or interest reinvestment plans, check the following box:

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the

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following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. o

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. o

If delivery of the prospectus is expected to be made pursuant to Rule 434, please check the following box. o

Title of each class of securities to be registered	Proposed maximum aggregate offering price (1)	Amount of registration fee (2)
Common Stock, par value \$0.01 per share, including preferred stock purchase rights	\$ 75,000,000	\$ 9,502.50

(1) Pursuant to Rule 457(o) under the Securities Act of 1933, as amended, the table does not specify the amount of shares of common stock to be registered or the proposed maximum aggregate price per share of common stock. The amount to be registered, the proposed maximum aggregate price per share and the proposed maximum aggregate offering price will be determined from time to time by us in connection with the issuance of the securities registered hereunder. In no event will the aggregate initial offering price of all securities issued from time to time pursuant to the prospectus contained in this registration statement exceed \$75,000,000.

(2) Calculated pursuant to Rule 457(o) under the Securities Act of 1933.

**The Registrant hereby amends this Registration Statement on such date or dates as may be necessary to delay its effective date until the Registrant shall file a further amendment which specifically states that this Registration Statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933 or until the Registration Statement shall become effective on such date as the SEC, acting pursuant to said Section 8(a), may determine.**

The information in this prospectus is not complete and may be changed. We may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities and it is not soliciting an offer to buy these securities in any state where the offer or sale is not permitted.

**Subject to Completion, dated December 9, 2004**

**PROSPECTUS**

**\$75,000,000**

**COMMON STOCK**

**[NEOSE TECHNOLOGIES, INC. LOGO]**

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 December 8, 2004, the reported last sale price of our common stock on The Nasdaq National Market was \$6.72 per share.

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

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**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.**

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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 \_\_\_\_\_, 2004.**

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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.

## 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.

## 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.

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 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.

***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;

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.

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 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.

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 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 collaborators' products, making it harder for us and our collaborators to realize an appropriate return.

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

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

Our research and development processes involve the controlled use of hazardous materials, chemicals, and radioactive compounds. We conduct experiments that are quite common in the biotechnology industry, in which we use small quantities of 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 \$14.00 per share in December 2002. During the past 12 months the price of our common stock has traded as low as \$6.45 per share in August 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;
- 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.

### **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.

### **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, plan, 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*

*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.*

### 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.

### 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 December 8, 2004, we had 24,717,171 shares of common stock outstanding and no shares of preferred stock outstanding. As of December 8, 2004, 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, 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 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 December 8, 2004, options to purchase a total of 5,114,742 shares of common stock have been granted and remain outstanding.

**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 reallocated 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 reallocate 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 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 makers 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.

***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.

**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.



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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 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](http://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.

**Part II****Information Not Required In Prospectus****Item 14. Other Expenses of Issuance and Distribution**

The following table sets forth the various expenses in connection with the sale and distribution of the securities being registered. All of the amounts shown are estimates except the Securities and Exchange Commission registration fee.

SEC registration fee	\$ 9,503
Legal fees and expenses	\$ 15,000
Accounting fees and expenses	\$ 5,000
Miscellaneous fees and expenses	\$ 5,000
	<hr/>
<b>TOTAL</b>	<b>\$ 34,503</b>

**Item 15. Indemnification of Directors and Officers**

Section 145 of the Delaware General Corporation Law ( Section 145 ) permits a corporation to indemnify any person who was or is a party or is threatened to be made a party to any threatened, pending or completed action, suit or proceeding, whether civil, criminal, administrative or investigative, by reason of the fact that he is or was a director, officer or agent of the corporation or another enterprise if serving at the request of the corporation. Depending on the character of the proceeding, a corporation may indemnify against expenses (including attorneys fees), judgments, fines and amounts paid in settlement actually and reasonably incurred in connection with such action, suit or proceeding if the person indemnified acted in good faith and, in respect to any criminal action or proceeding, had no reasonable cause to believe his conduct was unlawful. In the case of an action by or in the right of the corporation, no indemnification may be made with respect to any claim, issue or matter as to which such person shall have been adjudged to be liable to the corporation unless and only to the extent that the Court of Chancery or the court in which such action or suit was brought shall determine that, despite the adjudication of liability, such person is fairly and reasonably entitled to indemnity for such expenses which the court shall deem proper. Section 145 further provides that to the extent a director, officer, employee or agent of a corporation has been successful in the defense of any action, suit or proceeding referred to above, or in the defense of any claim, issue or matter therein, he shall be indemnified against expenses (including attorneys fees) actually and reasonably incurred by him in connection therewith.

Our certificate of incorporation limits the personal liability of directors to us or any of our stockholders for monetary damages for breach of fiduciary duty as a director, provided, however, that this limitation does not apply to any liability of a director (i) for any breach of the director s duty of loyalty to us or our stockholders, (ii) for acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of law, (iii) under Section 174 of Title 8 of the Delaware General Corporation Law, or (iv) for any transaction from which the director derived an improper personal benefit.

Section 6 of Article 7 of our second amended and restated by-laws provides to the fullest extent permitted by Section 145 for the indemnification of each person who was or is a party or is threatened to be made a party to any threatened, pending, or completed action, suit, or proceeding, whether civil, criminal, administrative, or investigative, by reason of the fact that he or she is or was, or has agreed to become, a director or officer of the corporation, or is or was serving, or has agreed to serve, at the request of the corporation, as a director, officer, or trustee of, or in a similar capacity with, another corporation, partnership, joint venture, trust, or other enterprise (including any employee benefit plan), or by reason of any action alleged to have been taken or omitted in such capacity, against all expenses (including attorneys fees), judgments, fines, and amounts paid in settlement actually and reasonably incurred by such person or on such person s behalf in connection with such action, suit, or proceeding and any appeal therefrom.

**Item 16. List of Exhibits**

The exhibits filed as part of this registration statement are as follows:

Exhibit	Description
1.1	Form of Underwriting Agreement.*
4.1	Third Amended and Restated Certificate of Incorporation (incorporated by reference to Exhibit 3.1 to our Current Report on Form 8-K filed with the SEC on May 14, 2004).
4.2	Second Amended and Restated By-Laws (incorporated by reference to Exhibit 3.2 to our Quarterly Report on Form 10-Q for the quarterly period ended September 30, 2002).
4.3	Certificate of Designation establishing and designating the Series A Junior Participating Preferred Stock (incorporated by reference to Exhibit 3.2 to our Current Report on Form 8-K filed with the SEC on October 1, 1997).
4.4	Amended and Restated Rights Agreement, dated as of December 3, 1998 between American Stock Transfer and Trust Company, as Rights Agent, and Neose Technologies, Inc. (incorporated by reference to Exhibit 4.1 to our Current Report on Form 8-K filed with the SEC on January 8, 1999).
4.5	Amendment No. 1, dated November 14, 2000 to the Amended and Restated Rights Agreement, dated as of December 3, 1998, between Neose Technologies, Inc. and American Stock Transfer and Trust Company, as Rights Agent (incorporated by reference to Exhibit 4.1 to our Current Report on Form 8-K filed with the SEC on November 15, 2000).
4.6	Amendment No. 2 dated June 13, 2002 to the Amended and Restated Rights Agreement, dated as of December 3, 1998, between Neose Technologies, Inc. and the American Stock Transfer & Trust Company, as Rights Agent (incorporated by reference to Exhibit 4.1 to our Current Report on Form 8-K filed with the SEC on June 13, 2002).
4.7	Amendment No. 3 dated October 30, 2002 to the Amended and Restated Rights Agreement, dated as of December 3, 1998, between Neose Technologies, Inc. and the American Stock Transfer & Trust Company, as Rights Agent (incorporated by reference to Exhibit 4.1 to our Current Report on Form 8-K filed with the SEC on November 1, 2002).
5.1	Opinion of Pepper Hamilton LLP regarding legality of securities being registered.
23.1	Consent of KPMG LLP.
23.2	Consent of Pepper Hamilton LLP (included in its opinion filed as Exhibit 5.1 hereto).
24.1	Powers of Attorney (included on signature page).

\*To be filed by amendment or by a report on Form 8-K pursuant to Regulation S-K, Item 601(b).

**Item 17. Undertakings**

The undersigned registrant hereby undertakes:

- (1) To file, during any period in which offers or sales are being made, a post-effective amendment to this Registration Statement:
  - (i) To include any prospectus required by Section 10(a)(3) of the Securities Act;
  - (ii) To reflect in the prospectus any facts or events arising after the effective date of the registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the registration statement. Notwithstanding the foregoing, any increase or decrease in the volume of the securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the Commission pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than 20 percent change in the maximum aggregate offering price set forth in the Calculation of Registration Fee table in the effective registration statement; and

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(iii) To include any material information with respect to the plan of distribution not previously disclosed in the registration statement or any material change to such information in the registration statement;

provided, however, that paragraphs (i) and (ii) above do not apply if the registration statement is on Form S-3 or Form S-8 and the information required to be included in a post-effective amendment by those paragraphs is contained in periodic reports filed by the registrant pursuant to Section 13 or Section 15(d) of the Exchange Act that are incorporated by reference in the registration statement

(2) That, for the purpose of determining any liability under the Securities Act, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof.

(3) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.

The undersigned Registrant hereby undertakes that, for purposes of determining any liability under the Securities Act, each filing of the Registrant's annual report pursuant to Section 13(a) or Section 15(d) of the Exchange Act that is incorporated by reference in the registration statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof.

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers and controlling persons of the registrant pursuant to the foregoing provisions or otherwise, the Registrant has been advised that in the opinion of the SEC such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the Registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question of whether such indemnification by it is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issue.

## SIGNATURES

Pursuant to the requirements of the Securities Act, Neose Technologies, Inc. certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and has duly caused this registration statement to be signed on its behalf by the undersigned, thereunto duly authorized in Horsham, Pennsylvania on December 9, 2004.

NEOSE TECHNOLOGIES, INC.

By:    /s/ C. BOYD CLARKE

**C. Boyd Clarke**  
**Chief Executive Officer**

## POWER OF ATTORNEY

Pursuant to the requirements of the Securities Act, this Registration Statement has been signed below by the following persons in the capacities and on the dates indicated. Each person whose signature appears below in so signing also makes, constitutes and appoints Debra J. Poul and A. Brian Davis, as his or her true and lawful attorney-in-fact and agent, with full power of substitution and resubstitution, for him or her and in his or her name, place and stead, in any and all capacities, to execute and cause to be filed with the Securities and Exchange Commission any and all amendments and post-effective amendments to this Registration Statement and a related registration statement that is to be effective upon filing pursuant to Rule 462(b) under the Securities Act, and in each case to file the same, with all exhibits thereto and other documents in connection therewith, and hereby ratifies and confirms all that said attorney-in-fact or his substitute or substitutes may do or cause to be done by virtue hereof. Pursuant to the requirements of the Securities Act, this registration statement has been signed by the following persons in the capacities and on the dates indicated.

Signature	Title	Date
<u>/s/ C. BOYD CLARKE</u>	President, Chief Executive Officer, (Principal Executive Officer) and Chairman of the Board of Directors	December 9, 2004
<b>C. Boyd Clarke</b>		
<u>/s/ ROBERT I. KRIEBEL</u>	Senior Vice President and Chief Financial Officer (Principal Financial Officer)	December 9, 2004
<b>Robert I. Kriebel</b>		
<u>/s/ BRIAN H. DOVEY</u>	Director	December 9, 2004
<b>Brian H. Dovey</b>		
<u>/s/ L. PATRICK GAGE</u>	Director	December 9, 2004
<b>L. Patrick Gage</b>		
<u>/s/ WILLIAM F. HAMILTON</u>	Director	December 9, 2004
<b>William F. Hamilton</b>		
<u>/s/ DOUGLAS J. MACMASTER</u>	Director	December 9, 2004
<b>Douglas J. McMaster, Jr.</b>		

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*/s/ MARK H. RACHESKY*

Director

December 9, 2004

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**Mark H. Rachesky**

*/s/ STEPHEN A. ROTH*

Director

December 9, 2004

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**Stephen A. Roth**

*/s/ LOWELL E. SEARS*

Director

December 9, 2004

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**Lowell E. Sears**

*/s/ ELIZABETH H.S. WYATT*

Director

December 9, 2004

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**Elizabeth H. S. Wyatt**

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Exhibit Index

<b>Exhibit</b>	<b>Description</b>
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