

Ceres, Inc.  
Form 4  
May 21, 2014

**FORM 4**

**UNITED STATES SECURITIES AND EXCHANGE COMMISSION  
Washington, D.C. 20549**

OMB APPROVAL

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Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

**STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP OF SECURITIES**

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934, Section 17(a) of the Public Utility Holding Company Act of 1935 or Section 30(h) of the Investment Company Act of 1940

(Print or Type Responses)

1. Name and Address of Reporting Person \*  
De Logi Walter Kamiel Marie

(Last) (First) (Middle)

1535 RANCHO CONEJO BOULEVARD

(Street)

THOUSAND OAKS, CA 91320

(City) (State) (Zip)

2. Issuer Name and Ticker or Trading Symbol  
Ceres, Inc. [CERE]

3. Date of Earliest Transaction (Month/Day/Year)  
04/30/2014

4. If Amendment, Date Original Filed(Month/Day/Year)

5. Relationship of Reporting Person(s) to Issuer

(Check all applicable)

Director  10% Owner  
 Officer (give title below)  Other (specify below)

6. Individual or Joint/Group Filing(Check Applicable Line)  
 Form filed by One Reporting Person  
 Form filed by More than One Reporting Person

**Table I - Non-Derivative Securities Acquired, Disposed of, or Beneficially Owned**

1. Title of Security (Instr. 3)	2. Transaction Date (Month/Day/Year)	2A. Deemed Execution Date, if any (Month/Day/Year)	3. Transaction Code (Instr. 8)	4. Securities Acquired (A) or Disposed of (D) (Instr. 3, 4 and 5)	5. Amount of Securities Beneficially Owned Following Reported Transaction(s) (Instr. 3 and 4)	6. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	7. Nature of Ownership (Instr. 4)
				(A) or (D) Price			
Common Stock	04/20/2014		G <sup>(1)</sup>	V 479,998 D \$ 0 0		D	
Common Stock					\$ 53,330	I	By wife

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

**Persons who respond to the collection of information contained in this form are not required to respond unless the form displays a currently valid OMB control number.**

SEC 1474 (9-02)

**Table II - Derivative Securities Acquired, Disposed of, or Beneficially Owned**  
*(e.g., puts, calls, warrants, options, convertible securities)*

1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative Security	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transaction Code (Instr. 8)	5. Number of Derivative Securities Acquired (A) or Disposed of (D) (Instr. 3, 4, and 5)	6. Date Exercisable and Expiration Date (Month/Day/Year)	7. Title and Amount of Underlying Securities (Instr. 3 and 4)	8. Price of Derivative Security (Instr. 5)	9. Number of Derivative Securities Owned Beneficially (Instr. 5)
				Code	V (A) (D)	Date Exercisable	Expiration Date	Title	Amount or Number of Shares

## Reporting Owners

### Reporting Owner Name / Address

### Relationships

Director 10% Owner Officer Other

De Logi Walter Kamiel Marie  
 1535 RANCHO CONEJO BOULEVARD X  
 THOUSAND OAKS, CA 91320

## Signatures

/s/ Walter De Logi 05/21/2014

\_\_Signature of Reporting Person Date

## Explanation of Responses:

- \* If the form is filed by more than one reporting person, see Instruction 4(b)(v).
- \*\* Intentional misstatements or omissions of facts constitute Federal Criminal Violations. See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

(1) The shares were given to an irrevocable trust for the benefit of the Reporting Person's family members.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure. Potential persons who are to respond to the collection of information contained in this form are not required to respond unless the form displays a currently valid OMB number. None of our product candidates has ever received regulatory approval to be marketed and sold in the United States or any other country. We may never receive regulatory approval for any of our product candidates.

*If the testing or use of our products harms people, we could be subject to costly and damaging product liability claims. We could also face costly and damaging claims arising from employment law, securities law, environmental law or other applicable laws governing our operations.*

The testing, manufacturing, marketing, and sale of drugs for use in people expose us to product liability risk. We are currently involved in a product liability lawsuit brought by a subject who participated in a clinical trial of one of our drug candidates. Any informed consent or waivers obtained from people who sign up for our clinical trials may not protect us from liability or the cost of litigation. Our product liability insurance may not cover all potential liabilities or may not completely cover any liability arising from any such litigation. Moreover, we may not have access to liability insurance or be able to maintain our insurance on acceptable terms.

## Edgar Filing: Ceres, Inc. - Form 4

In May 2003, securities class action lawsuits were commenced against us and certain of our officers and directors in the United States District Court for the Southern District of New York. A consolidated amended class action complaint was filed in October 2003. The complaint, which purports to be brought on behalf of a class consisting of investors in our publicly traded securities between March 28, 2000 and March 30, 2003, alleges that the defendants misstated or omitted material information concerning the safety and efficacy of AXOKINE, in violation of Sections 10(b) and 20(a) of the Securities and Exchange Act of 1934 and Rule 10b-5 promulgated thereunder. Damages are sought in an unspecified amount. We have not established a reserve for damages because we do not believe that a loss is probable. However, if the outcome of the litigation is adverse to us, we could be subject to significant liability, which could exceed our insurance coverage.

***Our operations may involve hazardous materials and are subject to environmental, health, and safety laws and regulations. We may incur substantial liability arising from our activities involving the use of hazardous materials.***

As a biopharmaceutical company with significant manufacturing operations, we are subject to extensive environmental, health, and safety laws and regulations, including those governing the use of hazardous materials. Our research and development and manufacturing activities involve the controlled use of chemicals, viruses, radioactive compounds, and other hazardous materials. The cost of compliance with environmental, health, and safety regulations is substantial. If an accident involving these materials or an environmental discharge were to occur, we could be held liable for any resulting damages, or face regulatory actions, which could exceed our resources or insurance coverage.

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### **Risks Related to Our Dependence on Third Parties**

***On February 27, 2004, Novartis Pharma AG provided notice to us that they would not participate in the continued development and commercialization of the IL-1 Trap under our collaboration agreement. This may harm our ability to develop and commercialize the IL-1 Trap.***

We relied heavily on Novartis to provide their expertise, resources, funding, manufacturing capacity, clinical expertise, and commercial infrastructure to support the IL-1 Trap program. Novartis' decision to withdraw from participating in the development and commercialization of the IL-1 Trap may delay or disrupt the IL-1 Trap program. We do not have the resources and skills to replace those of Novartis, which could result in significant delays in the development and potential commercialization of the IL-1 Trap. In addition, we will have to fund the development and commercialization of the IL-1 Trap without Novartis' long-term commitment, which will require substantially greater expenditures on our part.

***If our collaboration with Aventis Pharmaceuticals, Inc. for the VEGF Trap is terminated, our business operations and our ability to develop, manufacture, and commercialize the VEGF Trap in the time expected, or at all, would be harmed.***

We rely heavily on Aventis to assist with the development of the VEGF Trap. If the VEGF Trap program continues, we will rely on Aventis to assist with funding the VEGF Trap program, providing commercial manufacturing capacity, enrolling and monitoring clinical trials, obtaining regulatory approval, particularly outside the United States, and providing sales and marketing support. While we cannot assure you that the VEGF Trap will ever be successfully developed and commercialized, if Aventis does not perform its obligations in a timely manner, or at all, our ability to develop, manufacture, and commercialize the VEGF Trap will be significantly adversely affected. Aventis has the right to terminate its collaboration agreement with us at any time. If Aventis were to terminate its collaboration agreement with us, we might not have the resources or skills to replace those of our partner, which could cause significant delays in the development and/or manufacture of the VEGF Trap and result in substantial additional costs to us. We have no sales, marketing or distribution capabilities and would have to develop or outsource these capabilities. Termination of the Aventis collaboration agreement would create new and additional risks to the successful development of the VEGF Trap.

Sanofi-Synthelabo recently acquired Aventis, forming the sanofi-aventis Group. At present, it is unclear what impact, if any, this business combination will have on the VEGF Trap collaboration, including the possibility of a termination of the collaboration agreement and a delay in, or disruption to, the VEGF Trap development program.

***Our collaborators and service providers may fail to perform adequately in their efforts to support the development, manufacture, and commercialization of our drug candidates.***

We depend upon third-party collaborators, including Aventis and service providers such as clinical research organizations, outside testing laboratories, clinical investigator sites, and third party manufacturers and product packagers and labelers, to assist us in the development of our product candidates. If any of our existing collaborators or service providers breaches or terminates its agreement with us or does not perform its development or manufacturing services under an agreement in a timely manner or at all, we would experience additional costs, delays, and difficulties in the development or ultimate commercialization of our product candidates.

### **Risks Related to the Manufacture of Our Product Candidates**

***We have limited manufacturing capacity, which could inhibit our ability to successfully develop or commercialize our drugs.***

Before approving a new drug or biologic product, the FDA requires that the facilities at which the product will be manufactured be in compliance with current good manufacturing practices, or cGMP requirements. Manufacturing product candidates in compliance with these regulatory requirements is complex, time-

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consuming, and expensive. To be successful, our products must be manufactured for development, following approval, in commercial quantities, in compliance with regulatory requirements, and at competitive costs. If we or any of our product collaborators or third-party manufacturers, fillers or labelers are unable to maintain regulatory compliance, the FDA can impose regulatory sanctions, including, among other things, refusal to approve a pending application for a new drug or biologic product, or revocation of a pre-existing approval. As a result, our business, financial condition, and results of operations may be materially harmed.

Our manufacturing facility is likely to be inadequate to produce sufficient quantities of product for commercial sale. We intend to rely on our corporate collaborators, as well as contract manufacturers, to produce the large quantities of drug material needed for commercialization of our products. We rely entirely on third party manufacturers for filling and finishing services. We will have to depend on these manufacturers to deliver material on a timely basis and to comply with regulatory requirements. If we are unable to supply sufficient material on acceptable terms, or if we should encounter delays or difficulties in our relationships with our corporate collaborators or contract manufacturers, our business, financial condition, and results of operations may be materially harmed.

We may expand our own manufacturing capacity to support commercial production of active pharmaceutical ingredients, or API, for our product candidates. This will require substantial additional funds, and we will need to hire and train significant numbers of employees and managerial personnel to staff our facility. Start-up costs can be large and scale-up entails significant risks related to process development and manufacturing yields. We may be unable to develop manufacturing facilities that are sufficient to produce drug material for clinical trials or commercial use. In addition, we may be unable to secure adequate filling and finishing services to support our products. As a result, our business, financial condition, and results of operations may be materially harmed.

We may be unable to obtain key raw materials and supplies for the manufacture of our product candidates. In addition, we may face difficulties in developing or acquiring production technology and managerial personnel to manufacture sufficient quantities of our product candidates at reasonable costs and in compliance with applicable quality assurance and environmental regulations and governmental permitting requirements.

***If any of our clinical programs are discontinued, we may face costs related to the unused capacity at our manufacturing facilities.***

We maintain an 8,000 square foot manufacturing facility in Tarrytown, New York and have large-scale manufacturing operations in Rensselaer, New York. Under a long-term manufacturing agreement with Merck, which expires in October 2005 unless extended by mutual agreement, we produce an intermediate for a Merck pediatric vaccine at our facility in Rensselaer, New York. We also use our facilities to produce API for our own clinical and preclinical candidates. If we no longer use our facilities to manufacture the Merck intermediate or clinical candidates are discontinued, we would have to absorb overhead costs and inefficiencies.

***Certain of our raw materials are single-sourced from third parties; third-party supply failures could adversely affect our ability to supply our products.***

Certain raw materials necessary for manufacturing and formulation of our product candidates are provided by single-source unaffiliated third-party suppliers. We would be unable to obtain these raw materials for an indeterminate period of time if these third-party single-source suppliers were to cease or interrupt production or otherwise fail to supply these materials or products to us for any reason, including due to regulatory requirements or action, due to adverse financial developments at or affecting the supplier or due to labor shortages or disputes. This, in turn, could materially and adversely affect our ability to manufacture our product candidates for use in clinical trials, which could materially and adversely affect our operating results.

Also, certain of the raw materials required in the manufacturing and the formulation of our clinical candidates may be derived from biological sources, including mammalian tissues, bovine serum, and human serum albumin. There are certain European regulatory restrictions on using these biological source materials.

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If we are required to substitute these sources to comply with European regulatory requirements, our clinical development activities may be delayed or interrupted.

### **Risks Related to Commercialization of Products**

***If we are unable to establish sales, marketing, and distribution capabilities, or enter into agreements with third parties to do so, we will be unable to successfully market and sell future products.***

We have no sales or distribution personnel or capabilities and have only a small staff with marketing capabilities. If we are unable to obtain those capabilities, either by developing our own organizations or entering into agreements with service providers, we will not be able to successfully sell any products that we may bring to market in the future. In that event, we will not be able to generate significant revenue, even if our product candidates are approved. We cannot guarantee that we will be able to hire the qualified sales and marketing personnel we need or that we will be able to enter into marketing or distribution agreements with third-party providers on acceptable terms, if at all. Under the terms of our collaboration agreement with Aventis, we currently rely on Aventis for sales, marketing, and distribution of the VEGF Trap, should it be approved in the future by regulatory authorities for marketing. We will have to rely on a third party or devote significant resources to develop our own sales, marketing, and distribution capabilities for our other product candidates, and we may be unsuccessful in developing our own sales, marketing, and distribution organization.

***We may be unable to formulate or manufacture our product candidates in a way that is suitable for clinical or commercial use.***

Changes in product formulations and manufacturing processes may be required as product candidates progress in clinical development and are ultimately commercialized. If we are unable to develop suitable product formulations or manufacturing processes to support large scale clinical testing of our product candidates, including the VEGF Trap, IL-1 Trap, IL-4/13 Trap, and AXOKINE, we may be unable to supply necessary materials for our clinical trials, which would delay the development of our product candidates. Similarly, if we are unable to supply sufficient quantities of our product or develop product formulations suitable for commercial use, we will not be able to successfully commercialize our product candidates. For example, we are in the process of developing formulations that would allow delivery of higher doses of the IL-1 Trap to test in clinical trials. The dose levels that will be tested are substantially higher than the dose levels of other biological therapeutics currently approved for treatment of rheumatoid arthritis. Separate new formulations will be used for subcutaneous and intravenous administration of the higher dose therapeutic. If we are unable to develop or manufacture such a higher dose formulation that can be produced in a cost-effective manner, potential future IL-1 Trap sales and profitability may be limited.

***Even if our product candidates are ever approved, their commercial success is highly uncertain because our competitors may get to the marketplace before we do with better or lower cost drugs.***

There is substantial competition in the biotechnology and pharmaceutical industries from pharmaceutical, biotechnology, and chemical companies. Many of our competitors have substantially greater research, preclinical and clinical product development and manufacturing capabilities, and financial, marketing, and human resources than we do. Our smaller competitors may also enhance their competitive position if they acquire or discover patentable inventions, form collaborative arrangements or merge with large pharmaceutical companies. Even if we achieve product commercialization, our competitors have achieved, and may continue to achieve, product commercialization before our products are approved for marketing and sale. Genentech has an approved VEGF antagonist on the market and many different pharmaceutical and biotechnology companies are working to develop competing VEGF antagonists, including Novartis, Eyetech Pharmaceuticals, and Pfizer Inc. Many of these molecules are farther along in development than the VEGF Trap and may offer competitive advantages over our molecule. The marketing approval for Genentech's VEGF antagonist, Avastin<sup>®</sup>, may make it more difficult for us to enroll patients in clinical trials to support the VEGF Trap. This may delay or impair our ability to successfully develop and commercialize the VEGF Trap.

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The markets for both rheumatoid arthritis and asthma are both very competitive. Several highly successful medicines are available for these diseases. Examples include the TNF-antagonists Enbrel® (a registered trademark of Amgen Inc.), Remicade® (a registered trademark of Centocor Inc.), and Humira® (a registered trademark of Abbott Laboratories) for rheumatoid arthritis, and the leukotriene-modifier Singulair® (a registered trademark of Merck), as well as various inexpensive corticosteroid medicines for asthma. The availability of highly effective FDA approved TNF-antagonists makes it more difficult to successfully develop the IL-1 Trap for the treatment of rheumatoid arthritis, since it will be difficult to enroll patients with rheumatoid arthritis to participate in clinical trials of the IL-1 Trap. This may delay or impair our ability to successfully develop the drug candidate. In addition, even if the IL-1 Trap is ever approved for sale, it will be difficult for our drug to compete against these FDA approved TNF-antagonists because doctors and patients will have significant experience using these effective medicines. Moreover, these approved therapeutics may offer competitive advantages over the IL-1 Trap, such as requiring fewer injections. In addition, there are both small molecules and antibodies in development by third parties that are designed to block the synthesis of interleukin-1 or inhibit the signaling of interleukin-1. These drug candidates could offer competitive advantages over the IL-1 Trap. The successful development of these competing molecules could delay or impair our ability to successfully develop and commercialize the IL-1 Trap.

There is also substantial competition in the discovery and development of treatments for obesity, as well as established, cost-effective, and emerging surgical, prescription, and over-the-counter treatments for the disease that may offer competitive advantages over AXOKINE. AXOKINE is available only in injectable form, while the currently available marketed medicines for the treatment of obesity, and a late-stage product candidate in development by sanofi-aventis Group, are delivered in pill form, which is generally favored over injectable medicines. Therefore, even if AXOKINE is approved for sale, the fact that it must be delivered by injection may severely limit its market acceptance among patients and physicians.

***The successful commercialization of our product candidates will depend on obtaining coverage and reimbursement for use of these products from third-party payors.***

Sales of biopharmaceutical products largely depend on the reimbursement of patients' medical expenses by government health care programs and private health insurers. Without the financial support of the governments or third-party payors, the market for any biopharmaceutical product will be limited. These third-party payors increasingly challenge the price and examine the cost-effectiveness of products and services. Significant uncertainty exists as to the reimbursement status of any new therapeutic, particularly if there exist lower-cost standards of care. Third-party payors may not reimburse sales of our products, which would harm our business.

## **Risk Related to Employees**

***We are dependent on our key personnel and if we cannot recruit and retain leaders in our research, development, manufacturing, and commercial organizations, our business will be harmed.***

We are highly dependent on our executive officers. If we are not able to retain any of these persons or our Chairman, our business may suffer. In particular, we depend on the services of Roy Vagelos, M.D., the Chairman of our Board of Directors, Leonard Schleifer, M.D., Ph.D., our President and Chief Executive Officer, and George D. Yancopoulos, M.D., Ph.D., our Executive Vice President, Chief Scientific Officer and President, Regeneron Research Laboratories. There is intense competition in the biotechnology industry for qualified scientists and managerial personnel in the development, manufacture, and commercialization of drugs. We may not be able to continue to attract and retain the qualified personnel necessary for developing our business.

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### **Risks Related to Intellectual Property**

***If we cannot protect the confidentiality of our trade secrets or our patents are insufficient to protect our proprietary rights, our business and competitive position will be harmed.***

Our business requires using sensitive and proprietary technology and other information that we protect as trade secrets. We seek to prevent improper disclosure of these trade secrets through confidentiality agreements. If our trade secrets are improperly exposed, either by our own employees or our collaborators, it would help our competitors and adversely affect our business. We will be able to protect our proprietary rights from unauthorized use by third parties only to the extent that our rights are covered by valid and enforceable patents or are effectively maintained as trade secrets. The patent position of biotechnology companies involves complex legal and factual questions and, therefore, enforceability cannot be predicted with certainty. Our patents may be challenged, invalidated or circumvented. Patent applications filed outside the United States may be challenged by third parties who file an opposition. Such opposition proceedings are increasingly common in the European Union and are costly to defend. We have patent applications that are being opposed and it is likely that we will need to defend additional patent applications in the future. Our patent rights may not provide us with a proprietary position or competitive advantages against competitors. Furthermore, even if the outcome is favorable to us, the enforcement of our intellectual property rights can be expensive and time consuming.

***We may be restricted in our development and/or commercialization activities by third party patents.***

Our commercial success depends significantly on our ability to operate without infringing the patents and other proprietary rights of third parties. Other parties may allege that they have blocking patents to our Trap products in clinical development, either because they claim to hold proprietary rights to fusion proteins or proprietary rights to components of the Trap or the way it is manufactured. We are aware of certain United States and foreign patents relating to particular IL-4 and IL-13 receptors. Our IL-4/13 Trap includes portions of the IL-4 and IL-13 receptors. In addition, we are aware of a broad patent held by Genentech relating to proteins fused to certain immunoglobulin domains. Our Trap product candidates include proteins fused to immunoglobulin domains. Although we do not believe that we are infringing valid and enforceable third party patents, the holders of these patents may sue us for infringement and a court may find that we are infringing one or more validly issued patents, which may materially harm our business.

Any patent holders could sue us for damages and seek to prevent us from manufacturing, selling or developing our drug candidates, and a court may find that we are infringing validly issued patents of third parties. In the event that the manufacture, use or sale of any of our clinical candidates infringes on the patents or violates other proprietary rights of third parties, we may be prevented from pursuing product development, manufacturing, and commercialization of our drugs and may be required to pay costly damages. Such a result may materially harm our business, financial condition, and results of operations. Legal disputes are likely to be costly and time consuming to defend.

We seek to obtain licenses to patents when, in our judgment, such licenses are needed. If any licenses are required, we may not be able to obtain such licenses on commercially reasonable terms, if at all. The failure to obtain any such license could prevent us from developing or commercializing any one or more of our product candidates, which could severely harm our business.

### **Risks Related to Our Common Stock**

***Our stock price may be extremely volatile.***

There has been significant volatility in our stock price and generally in the market prices of biotechnology companies' securities. Various factors and events may have a significant impact on the market price of our common stock. These factors include, by way of example:

progress, delays or adverse results in clinical trials;

announcement of technological innovations or product candidates by us or competitors;



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fluctuations in our operating results;

public concern as to the safety or effectiveness of our product candidates;

developments in our relationship with collaborative partners;

developments in the biotechnology industry or in government regulation of healthcare;

large sales of our common stock by our executive officers, directors or significant shareholders;

arrivals and departures of key personnel; and

general market conditions.

The trading price of our common stock has been, and could continue to be, subject to wide fluctuations in response to these and other factors, including the sale or attempted sale of a large amount of our common stock in the market. Broad market fluctuations may also adversely affect the market price of our common stock.

***Future sales of our common stock by our significant shareholders or us may depress our stock price and impair our ability to raise funds in new share offerings.***

A small number of our shareholders beneficially own a substantial amount of our common stock. As of December 6, 2004, our six largest shareholders, which include Aventis and Novartis, beneficially owned 47.5% of our outstanding common shares, assuming, in the case of Leonard S. Schleifer, M.D., Ph.D, our chief executive officer, the exercise of all options held by him which are exercisable within 60 days of December 6, 2004. As of that date, Novartis owned 7,527,050 shares of common stock, representing approximately 13.5% of the common shares then outstanding. Under our registration rights agreement with Novartis, these shares of common stock may generally not be sold or otherwise transferred by Novartis until after March 28, 2005. As described under the caption Registration Rights of One of Our Shareholders found on page 15 of this prospectus, commencing after March 28, 2005, Novartis has certain registration rights with respect to these shares. As of December 6, 2004, Aventis owned 2,799,522 shares of common stock, representing approximately 5.0% of the common shares then outstanding. Under our stock purchase agreement with Aventis, these shares may generally not be sold or otherwise transferred until after September 5, 2005, and for one year after that date, Aventis may sell no more than 250,000 shares in any calendar quarter. After September 5, 2006, Aventis may sell no more than 500,000 shares in any calendar quarter. Accordingly, in 2005 and thereafter, as the restrictions on transfer applicable to the shares of common stock owned by Novartis and Aventis expire, these shares will be freely tradeable in the public market, subject, in the case of Aventis, to the foregoing continuing contractual sales volume restrictions. If Novartis or Aventis, or our other significant shareholders or we, sell substantial amounts of our common stock in the public market, or the perception that such sales may occur exists, the market price of our common stock could fall. Sales by our significant shareholders, including Aventis and Novartis, also might make it more difficult for us to raise funds by selling equity or equity-related securities in the future at a time and price that we deem appropriate.

***Our existing shareholders may be able to exert significant influence over matters requiring shareholder approval.***

Holders of Class A stock, who are the shareholders who purchased their stock from us before our initial public offering, are entitled to ten votes per share, while holders of common stock are entitled to one vote per share. As of December 6, 2004, holders of Class A stock held 4.2% of all shares of common stock and Class A stock then outstanding, and had 30.6% of the combined voting power of all common shares. These shareholders, if acting together, would be in a position to significantly influence the election of our directors and to effect or prevent certain corporate transactions that require majority or supermajority approval of the combined classes, including mergers and other business combinations. This may result in our company taking

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corporate actions that you may not consider to be in your best interest and may affect the price of our common stock. As of December 6, 2004:

our current officers and directors beneficially owned 14.8% of our outstanding common shares and 34.3% of the combined voting power of our common shares, assuming the exercise of all options held by such persons which are exercisable within 60 days of December 6, 2004; and

our six largest shareholders beneficially owned 47.5% of our outstanding common shares and 54.5% of the combined voting power of our common shares, assuming, in the case of Leonard S. Schleifer, M.D., Ph.D, our chief executive officer, the exercise of all options held by him which are exercisable within 60 days of December 6, 2004.

***The anti-takeover effects of provisions of our charter, by-laws and our rights agreement, and of New York corporate law, could deter, delay or prevent an acquisition or other change in control of us and could adversely affect the price of our common stock.***

Our amended and restated certificate of incorporation, our by-laws, our rights agreement and the New York Business Corporation Law contain various provisions that could have the effect of delaying or preventing a change in control of our company or our management that shareholders may consider favorable or beneficial. Some of these provisions could discourage proxy contests and make it more difficult for you and other shareholders to elect directors and take other corporate actions. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock. These provisions include:

authorization to issue blank check preferred stock, which is preferred stock that can be created and issued by the board of directors without prior shareholder approval, with rights senior to those of our common shareholders;

a staggered board of directors, so that it would take three successive annual meetings to replace all of our directors;

a requirement that removal of directors may only be effected for cause and only upon the affirmative vote of at least eighty percent (80%) of the outstanding shares entitled to vote for directors, as well as a requirement that any vacancy on the board of directors may be filled only by the remaining directors;

any action required or permitted to be taken at any meeting of shareholders may be taken without a meeting, only if, prior to such action, all of our shareholders consent, the effect of which is to require that shareholder action may only be taken at a duly convened meeting;

any shareholder seeking to bring business before an annual meeting of shareholders must provide timely notice of this intention in writing and meet various other requirements; and

under the New York Business Corporation Law, a plan of merger or consolidation of the Company must be approved by 2/3 of the votes of all outstanding shares entitled to vote thereon. See the risk factor immediately above captioned *Our existing shareholders may be able to exert significant influence over matters requiring shareholder approval.*

In addition, we have a shareholder rights plan which could make it more difficult for a third party to acquire us without the support of our board of directors and principal shareholders. See Description of Capital Stock-Rights Plan. In addition, many of our stock options issued under our 2000 Long-Term Incentive Plan may become fully vested in connection with a change in control of the Company, as defined in the plan.

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Unless otherwise stated in the applicable prospectus supplement, we intend to use the net proceeds of any securities sold by us to fund pre-clinical and clinical development of our product candidates, to fund basic research activities, to continue development of our technology platforms, for capital expenditures, to redeem, repay or purchase our 5 1/2% convertible senior subordinated notes due October 17, 2008, and for general corporate purposes, including working capital, acquisitions, and other business opportunities.

**RATIO OF EARNINGS TO COMBINED FIXED CHARGES AND  
PREFERRED STOCK DIVIDENDS**

The following table sets forth our ratio of earnings to combined fixed charges and preferred stock dividends, if any, for the periods presented. We had no preferred stock outstanding for any of these periods.

	Year Ended December 31,					Nine Months Ended
	1999	2000	2001	2002	2003	September 30, 2004
Ratio of earnings to combined fixed charges	(A)	(A)	(A)	(A)	(A)	4.43

(A) Due to our losses in the years ended December 31, 1999, 2000, 2001, 2002, and 2003, the ratio coverage was less than 1:1 for those periods. We would have needed to generate additional earnings of \$18.9 million, \$17.1 million, \$75.2 million, \$124.6 million, and \$107.6 million, for the years ended December 31, 1999, 2000, 2001, 2002, and 2003, respectively, to have achieved a coverage of 1:1.

For purposes of computing these ratios, earnings represents net income (loss) before income taxes plus fixed charges. Combined fixed charges represent interest expense, capitalized interest, amortization of deferred financing costs, and such portion of rental expense, deemed representative of the interest factor. The denominator is increased for preferred stock dividend requirements, if any, which represent the amount of pre-tax earnings required to cover such dividend requirements.

**DESCRIPTION OF SECURITIES**

This prospectus contains a summary of our common stock and Class A stock, preferred stock, debt securities, and warrants to purchase common stock, preferred stock, and debt securities. These summaries are not meant to be a complete description of each security. The particular terms of any security to be issued pursuant hereto will be set forth in a related prospectus supplement. This prospectus and the accompanying prospectus supplement will contain the material terms and conditions for each security.

**DESCRIPTION OF CAPITAL STOCK**

Our authorized capital stock consists of 160,000,000 shares of common stock, par value \$0.001 per share, 40,000,000 shares of Class A stock, par value \$0.001 per share, and 30,000,000 shares of preferred stock, par value \$0.01 per share. As of December 6, 2004, 53,384,650 shares of our common stock were outstanding and held by 621 shareholders of record and 2,358,373 shares of our Class A stock were outstanding and held by 56 shareholders of record. The following is a summary description of our capital stock. For more information, see our Restated Certificate of Incorporation dated June 21, 1991 and the amendments thereto.

*Common Stock and Class A Stock*

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*General.* The rights of holders of common stock and holders of Class A stock are identical except for voting rights, conversion rights, and restrictions on transferability.

*Voting Rights.* The holders of Class A stock are entitled to ten votes per share and the holders of common stock are entitled to one vote per share. Except as otherwise expressly provided by law, and subject to any voting rights provided to holders of preferred stock, holders of common shares have exclusive voting rights on all matters requiring a vote of shareholders. Except as provided by law, the holders of Class A stock and the holders of shares of common stock will vote together as a single class on all matters presented to the

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shareholders for their vote or approval, including the election of directors. Shareholders are not entitled to vote cumulatively for the election of directors and no class of outstanding common shares acting alone is entitled to elect any directors.

*Transfer Restrictions.* Class A stock is subject to certain limitations on transfer that do not apply to the common stock.

*Dividends and Liquidation.* Except as described in this paragraph, holders of Class A stock and holders of our common stock have an equal right to receive dividends when and if declared by our board of directors out of funds legally available therefor. If a dividend or distribution payable in Class A stock is made on the Class A stock, we must also make a pro rata and simultaneous dividend or distribution on the common stock payable in shares of common stock. Conversely, if a dividend or distribution payable in common stock is made on the common stock, we must also make a pro rata and simultaneous dividend or distribution on the Class A stock payable in shares of Class A stock. In the event of our liquidation, dissolution or winding up, holders of the shares of Class A stock and common stock are entitled to share equally, share-for-share, in the assets available for distribution after payment of all creditors and the liquidation preferences of our preferred stock.

*Optional Conversion Rights.* Each share of Class A stock may, at any time and at the option of the holder, be converted into one fully paid and nonassessable share of common stock. Upon conversion, such shares of common stock would not be subject to restrictions on transfer that applied to the shares of Class A stock prior to conversion except to the extent such restrictions are imposed under applicable securities laws. The shares of common stock are not convertible into or exchangeable for shares of Class A stock or any other of our shares or securities.

*Other Provisions.* Holders of Class A stock and common stock have no preemptive rights to subscribe for any additional securities of any class which we may issue and there are no redemption provisions or sinking fund provisions applicable to either such class, nor are our shares of Class A stock or the common stock subject to calls or assessments.

*Nasdaq National Market Listing.* Our common stock is quoted on the Nasdaq National Market. The current rules of the National Association of Securities Dealers, Inc. (the "NASD") effectively preclude the trading or quotation through the Nasdaq National Market of any securities of an issuer which has issued securities or taken other corporate action that would have the effect of nullifying, restricting or disparately reducing the per share voting of an outstanding class or classes of equity securities registered under section 12 of the Exchange Act. Certain national securities exchanges have adopted similar rules or policies. We do not intend to issue any additional shares of any stock that would make it ineligible for inclusion on the Nasdaq National Market or any national securities exchange. However, if we issue additional stock that causes us to become ineligible for continued inclusion on the Nasdaq National Market, then the ineligibility would be likely to materially reduce the liquidity of an investment in our common stock and would likely depress the market value of our common stock below that which would otherwise prevail.

*Transfer Agent and Registrar.* The transfer agent and registrar for our common stock is American Stock Transfer & Trust Company.

### ***Preferred Stock***

The following is a description of certain general terms and provisions of our preferred stock. The particular terms of any series of preferred stock will be described in a prospectus supplement and the extent, if any, to which the general provisions set forth below may apply to the series of preferred stock so offered will be described in the prospectus supplement. The following description of the preferred stock does not purport to be complete. You should refer to the provisions of our Restated Certificate of Incorporation dated June 21, 1991 and the amendments thereto, and to the Certificate of Amendment to our Restated Certificate of Incorporation relating to a specific series of preferred stock which will be in the form filed with the SEC as an exhibit to, or incorporated by reference in, the registration statement which includes this prospectus.

*General.* Our Restated Certificate of Incorporation allows us to issue up to 30,000,000 shares of preferred stock in one or more series and as may be determined by our board of directors. As of December 31, 2004, no shares of our preferred stock were outstanding and 100,000 shares of our Series A Junior

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Participating Preferred Stock were reserved for issuance in connection with our shareholders rights plan described below. Our board of directors has the authority, without shareholder consent, to establish from time to time the number of shares to be included in any series of our preferred stock, to fix the designation, powers, preference, and rights of the shares of any such series and any qualifications, limitations or restrictions thereof and to increase or decrease the number of shares of any such series without any further vote or action by the shareholders. The rights, preferences and restrictions of the preferred stock of any series of preferred stock will be fixed by a Certificate of Amendment to our Restated Certificate of Incorporation relating to such series. A prospectus supplement relating to such series will describe the terms of the preferred stock of the series, including the following:

the number of shares in that series;

the designation for that series by number, letter or title that shall distinguish the series from any other series of preferred stock;

the dividend rate (or method for determining the rate) for that series and whether dividends on that series of preferred stock will be cumulative, noncumulative or partially cumulative;

any liquidation preference per share of that series of preferred stock;

any conversion or exchange provisions applicable to that series of preferred stock;

any redemption or sinking fund provisions applicable to that series of preferred stock;

any voting rights of that series of preferred stock; and

the terms of any other preferences or rights applicable to that series of preferred stock.

*Permanent Global Preferred Securities.* A series of preferred stock may be issued in whole or in part in the form of one or more global securities that will be deposited with a depository or its nominee identified in the prospectus supplement relating to such series of preferred stock. The terms of the depository arrangement with respect to any series of preferred stock and the rights of and limitations on owners of beneficial interests in a global security representing a series of preferred stock will be described in the related prospectus supplement.

*Transfer Agent and Registrar.* The transfer agent and registrar for each series of preferred stock will be set forth in the prospectus supplement.

*Anti-Take-Over Effects.* Our board of directors may authorize, without shareholder approval, the issuance of preferred stock with voting and conversion rights that could adversely affect the voting power and other rights of holders of our common stock. Preferred stock could thus be issued quickly with terms designed to delay or prevent a change in control or to make the removal of management more difficult. In certain circumstances, this could have the effect of decreasing the market price of our common stock.

### ***Registration Rights of One of Our Shareholders***

One of our shareholders has registration rights. Under the registration rights agreement between us and such shareholder, after March 28, 2005, such shareholder (and certain of its transferees) may request that we file a registration statement under the Securities Act and, upon such request and subject to minimum size and other conditions, we will be required to use our best efforts to effect any such registration. We are not required to effect more than four such registrations. We are generally obligated to bear the expenses, other than underwriting discounts and sales commissions, of all of these registrations.

### ***Rights Plan***

*General.* In September 1996, we adopted a shareholder rights plan. Our rights agreement provides that each of our common shares will have attached to it one right which, when exercisable, entitles the registered

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holder upon exercise to purchase a unit consisting of one one-thousandth of a share of Series A junior participating preferred stock, par value \$.01 per share, at an initial purchase price of \$120 per unit, subject to customary antidilution adjustments. For a description of the terms of our Series A junior participating preferred stock, see Series A Junior Participating Preferred Stock below. Holders of rights will have no rights as shareholders, including the right to vote or receive dividends, simply by virtue of holding the rights.

*Exercisability of Rights.* The rights will not become exercisable until the earlier of:

ten days following a public announcement that a person or group (other than specified exempted persons) has become the beneficial owner of 20% or more of our common shares then outstanding; or

ten business days following the commencement of a tender or exchange offer that would result in a person or group becoming the beneficial owner of 20% or more of our common shares then outstanding.

*Flip-In Feature.* In the event a person or group (other than specified exempted persons) becomes the beneficial owner of 20% or more of our common shares then outstanding, other than pursuant to a tender or exchange offer for all outstanding common shares at a price and on other terms which a majority of our non-officer directors determine to be fair to and otherwise in the best interests of our shareholders, each right will entitle the holder (except for such person or group, whose rights will automatically become null and void) to acquire, upon exercise of the right, shares of our common stock having a value equal to twice the exercise price of the right. For example, if we assume that the initial purchase price of \$120 is in effect on the date that this flip-in feature of the right becomes applicable, each holder of a right, except for the person or group that has become the beneficial owner of 20% or more of our common shares then outstanding, can exercise a right by paying us \$120 in order to receive from us common stock having a value equal to \$240.

*Flip-Over Feature.* If, after a person or group (other than specified exempted persons) becomes the beneficial owner of 20% or more of our common shares, we engage in a merger or other business combination transaction and are not the surviving corporation, engage in a merger or other business combination in which we are the surviving corporation and our common shares are changed or exchanged, or 50% or more of our assets, cash flow or earning power is sold or transferred, then each holder of a right, except for the person or group that is the beneficial owner of 20% or more of our common shares then outstanding as described above, will have the right to receive, upon exercise of the right, shares of the acquiring company's capital stock having a value equal to twice the exercise price of the right.

*Redemption of Rights.* Our board of directors may redeem the rights, at a redemption price of \$.01 per right, at any time prior to the earlier of:

ten days following the public disclosure that a person or group (other than specified exempted persons) has become the beneficial owner of 20% or more of our common shares then outstanding, or

5:00 p.m. New York City time on October 18, 2006,

in which event the rights will terminate and the holders of the rights will have the right to receive only the redemption price for each right held.

*Amendment of Rights.* Except as described below in this paragraph, at any time before the rights become exercisable, our rights agreement may be supplemented or amended in any manner by our board of directors without the consent of the holders of common shares. After the rights become exercisable, except as described below in this paragraph, our board of directors may supplement or amend the rights agreement to cure any ambiguity, correct any defects, shorten or lengthen any time period, or make any other change that does not adversely affect the interests of holders of the rights (other than persons or groups (excluding specified exempted persons) beneficially owning 20% or more of our outstanding common shares), except that such no supplement or amendment may lengthen a time period relating to when the rights may be redeemed at a time when the rights are not redeemable or any other time period unless the lengthening is for the purpose of protecting, enhancing or clarifying the rights of, and/or the benefits to, the holders of the rights. In addition, no supplement or amendment of the rights agreement may change the redemption price for the rights, the final expiration date for the rights of October 18, 2006, the purchase price payable to exercise a right or the

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number of one one-thousandths of a share of Series A junior participating preferred stock for which a right is exercisable.

*Expiration of Rights.* If not previously exercised, the rights will expire at 5:00 p.m. New York City time on October 18, 2006, unless we redeem the rights earlier.

*Anti-Takeover Effects.* Our rights agreement may have anti-takeover effects. The rights may cause substantial dilution to a person or group that attempts to acquire us. Accordingly, the existence of the rights may deter acquirors from making takeover proposals or tender offers. However, the rights are not intended to prevent a takeover, but rather are designed to enhance the ability of our board to negotiate with an acquiror on behalf of all shareholders. The rights should not interfere with any merger or other business combination approved by our board of directors, since the board may redeem or amend the rights as described above, so that, in general, the rights would not be or become exercisable in connection with such an approved transaction. In addition, the rights should not interfere with a proxy contest.

*Series A Junior Participating Preferred Stock.* In connection with adopting our shareholder rights plan, our board of directors designated 100,000 shares of our authorized preferred stock as Series A junior participating preferred stock, none of which has been issued. Shares of our Series A junior participating preferred stock are issuable only if the rights become and continue to be exercisable, and are exercised, for Series A junior participating preferred stock in accordance with the rights agreement. If issued, each share of the Series A junior participating preferred stock:

will be nonredeemable and junior to all other series of preferred stock, unless otherwise provided in the terms of those other series of preferred stock;

will have a preferential quarterly dividend in an amount equal to the greater of \$.01 or 1,000 times the aggregate per share amount of cash and non-cash dividends declared on our common shares;

will have 1,000 votes, voting together with the common shares and any other capital stock with general voting rights; and

in the event of any merger, consolidation or other transaction in which common shares are converted or exchanged, will be entitled to receive 1,000 times the amount and type of consideration received per common share.

Upon and during specified dividend arrearages, the holders of Series A Participating Preferred Stock will also have the right, voting together as a single class with any other shares of preferred stock having such arrearages, to elect two directors. Upon liquidation, the holders of Series A junior participating preferred stock will be entitled to receive an aggregate preferred liquidation payment intended to equal 1000 times the then current purchase price payable to exercise a right, plus an amount equal to accrued and unpaid dividends and distributions on the Series A junior participating preferred stock, whether or not declared, to the date of such payment. The rights of our Series A junior participating preferred stock as to dividends, liquidation and voting, and in the event of mergers and consolidations, are protected by customary antidilution provisions.

### ***Anti-Takeover Effects of Provisions of the Charter and By-Laws, the Rights Agreement, and New York corporate law***

For a description of anti-takeover effects of various provisions of our charter, by-laws, our rights agreement and the New York Business Corporation Law, please see **RISK FACTORS Risks Related To Common Stock** *Our existing shareholders may be able to exert significant influence over matters requiring shareholder approval and The anti-takeover effects of provisions of our charter, by-laws and our rights agreement, and of New York corporate law, could defer, delay or prevent an acquisition or other change in control of us and could adversely affect the price of our common stock*, found on pages 11 and 12 of this prospectus, and the description of our rights plan in the immediately preceding section under the caption **Rights Plan**.



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**DESCRIPTION OF DEBT SECURITIES**

The following descriptions of the debt securities do not purport to be complete and are subject to and qualified in their entirety by reference to the indenture, a form of which has been filed with the SEC as an exhibit to the registration statement of which this prospectus is a part. Any future supplemental indenture or similar document also will be so filed. You should read the indenture and any supplemental indenture or similar document because they, and not this description, define your rights as holder of our debt securities. All capitalized terms have the meanings specified in the indenture.

We may issue, from time to time, debt securities, in one or more series, that will consist of either our senior debt ( Senior Debt Securities ), our senior subordinated debt ( Senior Subordinated Debt Securities ), our subordinated debt ( Subordinated Debt Securities ) or our junior subordinated debt ( Junior Subordinated Debt Securities and, together with the Senior Subordinated Debt Securities and the Subordinated Debt Securities, the Subordinated Securities ). The debt securities we offer will be issued under an indenture between us and one or more financial institutions qualified under the Trust Indenture Act to act as trustee. We may appoint more than one trustee under the indenture, each with respect to one or more series of debt securities. Each such trustee shall be a corporation or banking association organized and doing business in the United States that has a combined capital and surplus of at least \$10,000,000. Debt securities, whether senior, senior subordinated, subordinated or junior subordinated, may be issued as convertible debt securities or exchangeable debt securities.

***General Terms of the Indenture***

The indenture does not limit the amount of debt securities that we may issue. It provides that we may issue debt securities up to the principal amount that we may authorize and may be in any currency or currency unit designated by us. Except for the limitations on consolidation, merger, and sale of all or substantially all of our assets contained in the indenture, the terms of the indenture do not contain any covenants or other provisions designed to afford holders of any debt securities protection with respect to our operations, financial condition or transactions involving us.

We may issue the debt securities issued under the indenture as discount securities, which means they may be sold at a discount below their stated principal amount. These debt securities, as well as other debt securities that are not issued at a discount, may, for U.S. federal income tax purposes, be treated as if they were issued with original issue discount, or OID, because of interest payment and other characteristics. Special U.S. federal income tax considerations applicable to debt securities issued with original issue discount will be described in more detail in any applicable prospectus supplement.

The applicable prospectus supplement for a series of debt securities that we issue will describe, among other things, the following terms of the offered debt securities:

the title;

any limit on the aggregate principal amount;

whether issued in fully registered form without coupons or in a form registered as to principal only with coupons or in bearer form with coupons;

whether issued in the form of one or more global securities and whether all or a portion of the principal amount of the debt securities is represented thereby;

the price or prices at which the debt securities will be issued;

the date or dates on which principal is payable;

the place or places where and the manner in which principal, premium or interest will be payable and the place or places where the debt securities may be presented for transfer and, if applicable, conversion or exchange;

interest rates, and the dates from which interest, if any, will accrue, and the dates when interest is payable;

the right, if any, to extend the interest payment periods and the duration of the extensions;

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our rights or obligations to redeem or purchase the debt securities, including sinking fund or partial redemption payments;

conversion or exchange provisions, if any, including conversion or exchange prices or rates and adjustments thereto;

the currency or currencies of payment of principal or interest;

the terms applicable to any debt securities issued at a discount from their stated principal amount;

the terms, if any, pursuant to which any debt securities will be subordinate to any of our other debt;

if the amount of payments of principal or interest is to be determined by reference to an index or formula, or based on a coin or currency other than that in which the debt securities are stated to be payable, the manner in which these amounts are determined and the calculation agent, if any, with respect thereto;

if other than the entire principal amount of the debt securities when issued, the portion of the principal amount payable upon acceleration of maturity as a result of a default on our obligations;

if applicable, covenants affording holders of debt protection with respect to our operations, financial condition or transactions involving us; and

any other specific terms of any debt securities.

The applicable prospectus supplement will set forth certain U.S. federal income tax considerations for holders of any debt securities and the securities exchange or quotation system on which any debt securities are listed or quoted, if any.

Debt securities issued by us will be structurally subordinated to all indebtedness and other liabilities of our subsidiaries, except to the extent any such subsidiary guarantees or is otherwise obligated to make payment on such debt securities. As of December 6, 2004, we have no subsidiaries.

Unless otherwise provided in the applicable prospectus supplement, all securities of any one series need not be issued at the same time and may be issued from time to time without consent of any holder.

***Senior Debt Securities***

Payment of the principal of, premium, if any, and interest on Senior Debt Securities will rank on a parity with all of our other existing and future unsecured and unsubordinated debt.

***Senior Subordinated Debt Securities***

Payment of the principal of, premium, if any, and interest on Senior Subordinated Debt Securities will be junior in right of payment to the prior payment in full of all of our existing and future unsubordinated debt. We will set forth in the applicable prospectus supplement relating to any Senior Subordinated Debt Securities the subordination terms of such securities as well as the aggregate amount of outstanding debt, as of the most recent practicable date, that by its terms would be senior to the Senior Subordinated Debt Securities. We will also set forth in such prospectus supplement limitations, if any, on issuance of additional senior debt or additional senior subordinated debt.

***Subordinated Debt Securities***

Payment of the principal of, premium, if any, and interest on Subordinated Debt Securities will be subordinated and junior in right of payment to the prior payment in full of all of our senior and senior subordinated debt. We will set forth in the applicable prospectus supplement relating to any Subordinated Debt Securities the subordination terms of such securities as well as the aggregate amount of outstanding indebtedness, as of the most recent practicable date, that by its terms would be senior to the Subordinated Debt Securities. We will also set forth in such prospectus supplement limitations, if any, on issuance of additional senior debt, additional senior subordinated debt or additional subordinated debt.



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***Junior Subordinated Debt Securities***

Payment of the principal of, premium, if any, and interest on Junior Subordinated Debt Securities will be subordinated and junior in right of payment to the prior payment in full of all of our senior, senior subordinated, and subordinated debt. We will set forth in the applicable prospectus supplement relating to any Junior Subordinated Debt Securities the subordination terms of such securities as well as the aggregate amount of outstanding debt, as of the most recent practicable date, that by its terms would be senior to the Junior Subordinated Debt Securities. We will also set forth in such prospectus supplement limitations, if any, on issuance of additional debt.

***Conversion or Exchange Rights***

Debt securities may be convertible into or exchangeable for our other securities or property. The terms and conditions of conversion or exchange will be set forth in the applicable prospectus supplement. The terms will include, among others, the following:

the conversion or exchange price;

the conversion or exchange period;

provisions regarding the ability of us or the holder to convert or exchange the debt securities;

events requiring adjustment to the conversion or exchange price; and

provisions affecting conversion or exchange in the event of our redemption of the debt securities.

***Consolidation, Merger or Sale***

We cannot consolidate or merge with or into, or transfer or lease all or substantially all of our assets to, any person (other than a direct or indirect wholly owned subsidiary of the Issuer) unless (a) we will be the continuing corporation or (b) the successor corporation or person to which our assets are transferred or leased is a corporation organized under the laws of the United States, any state of the United States or the District of Columbia and it expressly assumes our obligations on the debt securities and under the indenture. In addition, we cannot effect such a transaction unless immediately after giving effect to such transaction, no default or event of default under the indenture shall have occurred and be continuing. Subject to certain exceptions, when the person to whom our assets are transferred or leased has assumed our obligations under the debt securities and the indenture, we shall be discharged from all of our obligations under the debt securities and the indenture.

This covenant would not apply to any recapitalization transaction, a change of control of our company or a highly leveraged transaction, unless the transaction or change of control were structured to include a merger or consolidation or transfer or lease of all or substantially all of our assets.

***Events of Default***

Unless otherwise indicated, the term **Event of Default**, when used in the indenture in respect of a series of debt securities, means any of the following:

failure to pay interest on any debt security of such series for 30 days after the date payment is due and payable, provided that an extension of an interest payment period by us in accordance with the terms of the debt securities of such series shall not constitute a failure to pay interest;

failure to pay principal or premium, if any, on any debt security of such series when due, either at maturity, upon any redemption, by declaration or otherwise;

failure to make sinking fund payments in respect of any debt security of such series when due;

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failure to perform any other covenant contained in the indenture (other than a covenant in the indenture solely for the benefit of a different series of debt securities) for 90 days after we receive

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written notice that performance is required from the trustee or the holders of at least 25% in aggregate principal amount of the debt securities of such series then outstanding;

events in bankruptcy, insolvency or reorganization of our company; or

any other Event of Default provided in the applicable resolution of our board of directors or the supplemental indenture under which we issue such series of debt securities.

An Event of Default for a particular series of debt securities does not necessarily constitute an Event of Default for any other series of debt securities issued under the indenture. If an Event of Default relating to the payment of interest, principal or any sinking fund installment involving any series of debt securities has occurred and is continuing, the trustee or the holders of not less than 25% in aggregate principal amount of the debt securities of each affected series then outstanding may declare the entire principal of all the debt securities of that series to be due and payable immediately.

If an Event of Default relating to the performance of other covenants in the indenture occurs and is continuing for a period of 90 days after notice of such, or if any other Event of Default provided in a supplemental indenture or board resolution occurs and is continuing, and such Event of Default involves all of the series of Senior Debt Securities, then the trustee or the holders of not less than 25% in aggregate principal amount of all of the series of Senior Debt Securities then outstanding (treated as one class) may declare the entire principal amount of all of the series of Senior Debt Securities due and payable immediately.

Similarly, if an Event of Default relating to the performance of other covenants in the indenture occurs and is continuing for a period of 90 days after notice of such, or if any other Event of Default provided in a supplemental indenture or board resolution occurs and is continuing, and such Event of Default involves all of the series of Subordinated Securities, then the trustee or the holders of not less than 25% in aggregate principal amount of all of the series of Subordinated Securities may declare the entire principal amount of all of the series of Subordinated Securities due and payable immediately.

If, however, the Event of Default relating to the performance of other covenants in the indenture or any other Event of Default provided in a supplemental indenture or board resolution that has occurred and is continuing is for less than all of the series of Senior Debt Securities or Subordinated Securities, as the case may be, then, the trustee or the holders of not less than 25% in aggregate principal amount of each affected series of the Senior Debt Securities or the Subordinated Securities, as the case may be, may declare the entire principal amount of all debt securities of such affected series due and payable immediately. The holders of not less than a majority in aggregate principal amount of the debt securities of a series may, after satisfying conditions, rescind and annul any of the above-described declarations and consequences involving the series.

If an Event of Default relating to events in bankruptcy, insolvency or reorganization of our company occurs and is continuing, then the principal amount of all of the debt securities outstanding under the indenture, and any accrued interest, will automatically become due and payable immediately, without any declaration or other act by the trustee or any holder.

The indenture imposes limitations on suits brought by holders of debt securities against us. Except as provided below, no holder of debt securities of any series may institute any action against us under the indenture unless:

the holder has previously given to the trustee written notice of default and continuance of that default;

the holders of at least 25% in principal amount of the outstanding debt securities of the affected series have requested that the trustee institute the action;

the requesting holders have offered the trustee reasonable indemnity for expenses and liabilities that may be incurred by bringing the action;

the trustee has not instituted the action within 60 days of the request; and

the trustee has not received inconsistent direction by the holders of a majority in principal amount of the outstanding debt securities of the series.

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Notwithstanding the foregoing, each holder of debt securities of any series has the right, which is absolute and unconditional, to receive payment of the principal of and premium and interest, if any, on such debt securities when due and to institute suit for the enforcement of any such payment, and such rights may not be impaired without the consent of that holder of debt securities.

We will be required to file annually with the trustee a certificate, signed by an officer of our company, stating whether or not the officer knows of any default by us in the performance, observance or fulfillment of any condition or covenant of the indenture.

***Registered Global Securities***

We may issue the debt securities of a series in whole or in part in the form of one or more fully registered global securities that we will deposit with a depository or with a nominee for a depository identified in the applicable prospectus supplement and registered in the name of such depository or nominee. In such case, we will issue one or more registered global securities denominated in an amount equal to the aggregate principal amount of all of the debt securities of the series to be issued and represented by such registered global security or securities.

Unless and until it is exchanged in whole or in part for debt securities in definitive registered form, a registered global security may not be transferred except as a whole:

by the depository for such registered global security to its nominee;

by a nominee of the depository to the depository or another nominee of the depository; or

by the depository or its nominee to a successor of the depository or a nominee of the successor.

The prospectus supplement relating to a series of debt securities will describe the specific terms of the depository arrangement with respect to any portion of such series represented by a registered global security. We anticipate that the following provisions will apply to all depository arrangements for debt securities:

ownership of beneficial interests in a registered global security will be limited to persons that have accounts with the depository for the registered global security, those persons being referred to as participants, or persons that may hold interests through participants;

upon the issuance of a registered global security, the depository for the registered global security will credit, on its book-entry registration and transfer system, the participants' accounts with the respective principal amounts of the debt securities represented by the registered global security beneficially owned by the participants;

any dealers, underwriters or agents participating in the distribution of the debt securities will designate the accounts to be credited; and

ownership of any beneficial interest in the registered global security will be shown on, and the transfer of any ownership interest will be effected only through, records maintained by the depository for the registered global security (with respect to interests of participants) and on the records of participants (with respect to interests of persons holding through participants).

The laws of some states may require that certain purchasers of securities take physical delivery of the securities in definitive form. These laws may limit the ability of those persons to own, transfer or pledge beneficial interests in registered global securities.

So long as the depository for a registered global security, or its nominee, is the registered owner of the registered global security, the depository or the nominee, as the case may be, will be considered the sole owner or holder of the debt securities represented by the registered global security for all purposes under the indenture. Except as set forth below, owners of beneficial interests in a registered global security:

will not be entitled to have the debt securities represented by a registered global security registered in their names;



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will not receive or be entitled to receive physical delivery of the debt securities in the definitive form; and

will not be considered the owners or holders of the debt securities under the indenture.

Accordingly, each person owning a beneficial interest in a registered global security must rely on the procedures of the depository for the registered global security and, if the person is not a participant, on the procedures of a participant through which the person owns its interest, to exercise any rights of a holder under the indenture.

We understand that under existing industry practices, if we request any action of holders or if an owner of a beneficial interest in a registered global security desires to give or take any action that a holder is entitled to give or take under the indenture, the depository for the registered global security would authorize the participants holding the relevant beneficial interests to give or take the action, and those participants would authorize beneficial owners owning through those participants to give or take the action or would otherwise act upon the instructions of beneficial owners holding through them.

We will make payments of principal and premium, if any, and interest, if any, on debt securities represented by a registered global security registered in the name of a depository or its nominee to the depository or its nominee, as the case may be, as the registered owners of the registered global security. None of our company, the trustee or any other agent of our company or the trustee will be responsible or liable for any aspect of the records relating to, or payments made on account of, beneficial ownership interests in the registered global security or for maintaining, supervising or reviewing any records relating to the beneficial ownership interests.

We expect that the depository for any debt securities represented by a registered global security, upon receipt of any payments of principal and premium, if any, and interest, if any, in respect of the registered global security, will immediately credit participants' accounts with payments in amounts proportionate to their respective beneficial interests in the registered global security as shown on the records of the depository. We also expect that standing customer instructions and customary practices will govern payments by participants to owners of beneficial interests in the registered global security held through the participants, as is now the case with the securities held for the accounts of customers in bearer form or registered in street name. We also expect that any of these payments will be the responsibility of the participants.

If the depository for any debt securities represented by a registered global security is at any time unwilling or unable to continue as depository or ceases to be a clearing agency registered under the Exchange Act, we will appoint an eligible successor depository. If we fail to appoint an eligible successor depository within 90 days, we will issue the debt securities in definitive form in exchange for the registered global security. In addition, we may at any time and in our sole discretion decide not to have any of the debt securities of a series represented by one or more registered global securities. In such event, we will issue debt securities of that series in a definitive form in exchange for all of the registered global securities representing the debt securities. The trustee will register any debt securities issued in definitive form in exchange for a registered global security in such name or names as the depository, based upon instructions from its participants, shall instruct the trustee.

We may also issue bearer debt securities of a series in the form of one or more global securities, referred to as bearer global securities. We will deposit these bearer global securities with a common depository for Euroclear System and Clearstream Bank Luxembourg, Societe Anonyme, or with a nominee for the depository identified in the prospectus supplement relating to that series. The prospectus supplement relating to a series of debt securities represented by a bearer global security will describe the specific terms and procedures, including the specific terms of the depository arrangement and any specific procedures for the issuance of debt securities in definitive form in exchange for a bearer global security, with respect to the position of the series represented by a bearer global security.

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***Discharge, Defeasance, and Covenant Defeasance***

We can discharge or defease our obligations under the indenture as set forth below. Unless otherwise set forth in the applicable prospectus supplement, the subordination provisions applicable to any Subordinated Securities will be expressly made subject to the discharge and defeasance provisions of the indenture.

We may discharge some of our obligations to holders of any series of debt securities that have not already been delivered to the trustee for cancellation and that have either become due and payable or are by their terms to become due and payable within one year (or are scheduled for redemption within one year). We may effect a discharge by irrevocably depositing with the trustee cash or U.S. government obligations, as trust funds, in an amount certified to be sufficient to pay when due, whether at maturity, upon redemption or otherwise, the principal of, premium, if any, and interest on the debt securities, and any mandatory sinking fund payments.

Unless otherwise provided in the applicable prospectus supplement, we may also discharge any and all of our obligations to holders of any series of debt securities at any time ( defeasance ). We also may be released from the obligations imposed by any covenants of any outstanding series of debt securities and provisions of the indenture, and we may omit to comply with those covenants without creating an Event of Default ( covenant defeasance ). We may effect defeasance and covenant defeasance only if, among other things:

we irrevocably deposit with the trustee cash or U.S. government obligations, as trust funds, in an amount certified to be sufficient to pay at maturity (or upon redemption) the principal, premium, if any, and interest on all outstanding debt securities of the series; and

we deliver to the trustee an opinion of counsel from a law firm to the effect that the holders of the series of debt securities will not recognize income, gain or loss for U.S. federal income tax purposes as a result of the defeasance or covenant defeasance and that defeasance or covenant defeasance will not otherwise alter the holders' U.S. federal income tax treatment of principal, premium, if any, and interest payments on the series of debt securities, which opinion, in the case of legal defeasance, must be based on a ruling of the Internal Revenue Service issued or a change in U.S. federal income tax law.

Although we may discharge or defease our obligations under the indenture as described in the two preceding paragraphs, we may not avoid, among other things, our duty to register the transfer or exchange of any series of debt securities, to replace any temporary, mutilated, destroyed, lost or stolen series of debt securities or to maintain an office or agency in respect of any series of debt securities.

***Modification of the Indenture***

The indenture provides that we and the trustee may enter into supplemental indentures without the consent of the holders of debt securities of a series to:

secure our obligations under debt securities of such series;

evidence the assumption by a successor corporation of our obligations;

add covenants for the protection of the holders of debt securities of such series, and to make the occurrence or continuance of a default in any such additional covenants an Event of Default;

surrender any right, power or option conferred upon us in respect of debt securities of such series;

if debt securities of the series are convertible, to provide for conversion rights of holders of such debt securities if any reclassification or change of our common stock or any consolidation, merger or sale of all or substantially all of our assets occurs;

make any change to comply with the Trust Indenture Act, as amended, or any requirement of the SEC in connection with the qualification of the indenture under the Trust Indenture Act of 1939, as amended;

cure any ambiguity or correct any defect or inconsistency in the indenture;

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make any change that does not adversely affect the rights of holders of debt securities of such series in any material respect;

establish the forms or terms of debt securities of any series;

evidence and provide for the acceptance of appointment by a successor trustee; and

to change or eliminate any provision, or to add any new provision, in respect of one or more series of securities; provided such change, elimination or addition does not apply to any outstanding security.

The indenture also provides that we and the trustee may, with the consent of the holders of not less than a majority in aggregate principal amount of debt securities of all series of Senior Debt Securities (voting as one class) or of all series of Subordinated Securities (voting as one series), as the case may be, then outstanding and affected, add any provisions to, or change in any manner, eliminate or modify in any way the provisions of, the indenture or modify in any manner the rights of the holders of the debt securities of each such series. We and the trustee may not, however, without the consent of the holder of each outstanding debt security affected thereby:

extend the final maturity of any debt security;

reduce the principal amount or premium, if any, of any debt security;

reduce the rate or extend the time of payment of interest on any debt security;

reduce any amount payable on redemption on any debt security;

change the currency in which the principal (other than as may be provided otherwise with respect to a series), premium, if any, or interest is payable in respect of any debt security;

reduce the amount of the principal of any debt security issued with an OID that is payable upon acceleration or provable in bankruptcy;

modify any of the subordination provisions or the definition of senior indebtedness applicable to any Subordinated Securities in a manner adverse to the holders of those securities;

alter provisions of the indenture relating to the debt securities not denominated in U.S. dollars;

impair the right to institute suit for the enforcement of any payment on any debt security when due; or

reduce the percentage of holders of debt securities of any series whose consent is required for any modification of the indenture.

***Concerning the Trustee***

The indenture provides that there may be more than one trustee under the indenture, each with respect to one or more series of debt securities. If there are different trustees for different series of debt securities, each trustee will be a trustee of a trust under the indenture separate and apart from the trust administered by any other trustee under the indenture. Except as otherwise indicated in this prospectus or any prospectus supplement, any action permitted to be taken by a trustee may be taken by such trustee only with respect to the one or more series of debt securities for which it is the trustee under the indenture. Any trustee under the indenture may resign or be removed with respect to one or more series of debt securities. All payments of principal of, premium, if any, and interest on, and all registration, transfer, exchange, authentication, and delivery of (including authentication and delivery on original issuance of the debt securities), the debt securities of a series (other than debt securities issued in bearer form) will be effected by the trustee with respect to that series at an office designated by the trustee in New York, New York.

The indenture contains limitations on the right of the trustee, should it become a creditor of our company, to obtain payment of claims in some cases or to realize on certain property received in respect of any such claim as security or otherwise. The trustee may engage in other transactions. If it acquires any conflicting interest relating to any duties with respect to the debt securities, however, it must eliminate the conflict or resign as trustee.



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The holders of a majority in aggregate principal amount of any series of debt securities then outstanding will have the right to direct the time, method, and place of conducting any proceeding for exercising any remedy available to the trustee with respect to such series of debt securities, provided that the direction would not conflict with any rule of law or with the indenture, would not be unduly prejudicial to the rights of another holder of the debt securities, and would not involve any trustee in personal liability. The indenture provides that if an Event of Default shall occur and be known to any trustee and not be cured, the trustee must use the same degree of care as a prudent person would use in the conduct of his or her own affairs in the exercise of the trustee's power. Subject to these provisions, the trustee will be under no obligation to exercise any of its rights or powers under the indenture at the request of any of the holders of the debt securities, unless they shall have offered to the trustee security and indemnity satisfactory to the trustee.

### ***No Individual Liability of Incorporators, Shareholders, Officers or Directors***

The indenture provides that neither our incorporator nor any of our past, present or future shareholders, officers or directors of our company or any successor corporation in their capacity as such shall have any individual liability for any of our obligations, covenants or agreements under the debt securities or the indenture.

### ***Governing Law***

The indenture and the debt securities will be governed by, and construed in accordance with, the laws of the State of New York.

## **DESCRIPTION OF WARRANTS**

### ***General***

We may issue warrants for the purchase of debt securities, preferred stock or common stock, or any combination thereof. Warrants may be issued independently or together with debt securities, preferred stock or common stock and may be attached to or separate from any offered securities. Warrants may be issued under warrant agreements issued to the holders thereof. Alternatively, one or more series of warrants may be issued under a separate warrant agreement to be entered into between us and a bank or trust company, as warrant agent. Any such warrant agent will act solely as our agent in connection with the warrants and will not have any obligation or relationship of agency or trust for or with any holders or beneficial owners of warrants. This summary of certain provisions of the warrants is not complete. For the complete terms of a particular series of warrants, you should refer to the prospectus supplement for that series of warrants and the warrant agreement for that particular series.

### ***Debt Warrants***

The prospectus supplement relating to a particular issue of warrants to purchase debt securities will describe the terms of the debt warrants, including the following:

the title of the debt warrants;

the offering price for the debt warrants, if any;

the aggregate number of the debt warrants;

the designation and terms of the debt securities, including any conversion rights, purchasable upon exercise of the debt warrants;

if applicable, the date from and after which the debt warrants and any debt securities issued with them will be separately transferable;

the principal amount of debt securities that may be purchased upon exercise of a debt warrant and the exercise price for the warrants, which may be payable in cash, securities or other property;

the dates on which the right to exercise the debt warrants will commence and expire;

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if applicable, the minimum or maximum amount of the debt warrants that may be exercised at any one time;

whether the debt warrants, represented by the debt warrant certificates or debt securities that may be issued upon exercise of the debt warrants, will be issued in registered or bearer form;

information with respect to book-entry procedures, if any;

the currency or currency units in which the offering price, if any, and the exercise price are payable;

the redemption or call provisions, if any, applicable to the debt warrants; and

any additional terms of the debt warrants, including terms, procedures, and limitations relating to the exchange, exercise, and settlement of the debt warrants.

Debt warrant certificates will be exchangeable for new debt warrant certificates of different denominations. Debt warrants may be exercised at the corporate trust office of the warrant agent or any other office indicated in the debt warrant certificate or the related prospectus supplement. Prior to the exercise of their debt warrants, holders of debt warrants will not have any of the rights of holders of the debt securities purchasable upon exercise and will not be entitled to payment of principal or any premium, if any, or interest on the debt securities purchasable upon exercise.

***Stock Warrants***

The prospectus supplement relating to a particular series of warrants to purchase our common stock or preferred stock will describe the terms of the warrants, including the following:

the title of the warrants;

the offering price for the warrants, if any;

the aggregate number of the warrants;

the designation and terms of the common stock or preferred stock that may be purchased upon exercise of the warrants;

if applicable, the designation and terms of the securities with which the warrants are issued and the number of warrants issued with each security;

if applicable, the date from and after which the warrants and any securities issued with the warrants will be separately transferable;

the number of shares of common stock or preferred stock that may be purchased upon exercise of a warrant and the exercise price for the warrants;

the dates on which the right to exercise the warrants shall commence and expire;

if applicable, the minimum or maximum amount of the warrants that may be exercised at any one time;

the currency or currency units in which the offering price, if any, and the exercise price are payable;

the antidilution provisions of the warrants, if any;

the redemption or call provisions, if any, applicable to the warrants; and

any additional terms of the warrants, including terms, procedures, and limitations relating to the exchange, exercise, and settlement of the warrants.

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Holders of stock warrants will not be entitled:

to vote, consent or receive dividends;

receive notice as shareholders with respect to any meeting of shareholders for the election of our directors or any other matter; or

exercise any rights as shareholders of our company.



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**PLAN OF DISTRIBUTION**

We may sell debt securities, common stock, preferred stock or warrants to purchase debt securities, common stock or preferred stock in one or more of the following ways from time to time:

to or through underwriters or dealers;

by ourself directly;

through agents; or

through a combination of any of these methods of sale.

A prospectus supplement relating to an offering of offered securities will set forth the terms of such offering, including:

the name or names of any underwriters, dealers or agents;

the purchase price of the offered securities and the proceeds to us from the sale;

any underwriting discounts and commissions or agency fees and other items constituting underwriters or agents compensation; and

any initial public offering price, any discounts or concessions allowed or reallocated or paid to dealers, and any securities exchanges on which such offered securities may be listed.

Any initial public offering prices, discounts or concessions allowed or reallocated or paid to dealers may be changed from time to time.

If underwriters are used in the sale, the underwriters may acquire the offered securities for their own account and may resell them from time to time 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 offered securities may be offered either to the public through underwriting syndicates represented by one or more managing underwriters or by one or more underwriters without a syndicate. Unless otherwise set forth in a prospectus supplement, any obligation of the underwriters to purchase any series of securities will be subject to certain conditions precedent.

In connection with underwritten offerings of the offered securities and in accordance with applicable law and industry practice, underwriters may over-allot or effect transactions that stabilize, maintain or otherwise affect the market price of the offered securities at levels above those that might otherwise prevail in the open market, including by entering stabilizing bids, effecting syndicate covering transactions or imposing penalty bids, each of which is described below.

A stabilizing bid means the placing of any bid, or the effecting of any purchase, for the purpose of pegging, fixing or maintaining the price of a security.

A syndicate covering transaction means the placing of any bid on behalf of the underwriting syndicate or the effecting of any purchase to reduce a short position created in connection with the offering.

A penalty bid means an arrangement that permits the managing underwriter to reclaim a selling concession from a syndicate member in connection with the offering when offered securities originally sold by the syndicate member are purchased in syndicate covering transactions.

These transactions may be effected on the Nasdaq National Market, in the over-the-counter market or otherwise. Underwriters are not required to engage in any of these activities, or to continue such activities if commenced.

If a dealer is used in the sale, we may sell such offered securities to the dealer, as principal. The dealer may then resell the offered securities to the public at varying prices to be determined by that dealer at the time for resale. The names of the dealers and the terms of the transaction will be set forth in the prospectus supplement relating to that transaction.



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Offered securities may be sold directly by us to one or more institutional purchasers, or through agents designated by us, from time to time, at a fixed price or prices, which may be changed, or at varying prices determined at the time of sale. Any agent involved in the offer or sale of the offered securities in respect of which this prospectus is delivered will be named, and any commissions payable by us to such agent will be set forth, in the prospectus supplement relating to that offering. Unless otherwise indicated in such prospectus supplement, any such agent will be acting on a best efforts basis for the period of its appointment.

Underwriters, dealers, and agents may be entitled under agreements entered into with us to indemnification by us against certain civil liabilities, including liabilities under the Securities Act, or to contribution with respect to payments that the underwriters, dealers or agents may be required to make in respect thereof. Underwriters, dealers, and agents may be customers of, engage in transactions with, or perform services for us and our affiliates from time to time in the ordinary course of business.

Other than our common stock, which is listed on the Nasdaq National Market, each of the securities issued hereunder will be a new issue of securities, will, unless otherwise indicated in the relevant prospectus supplement, have no prior trading market, and may or may not be listed on a national securities exchange or the Nasdaq National Market. Any common stock sold pursuant to a prospectus supplement will be listed on the Nasdaq National Market, subject to official notice of issuance. Any underwriters to whom we sell securities for public offering and sale may make a market in the securities, but such underwriters will not be obligated to do so and may discontinue any market making at any time without notice. We cannot assure you that there will be a market for the offered securities.

**LEGAL MATTERS**

The validity of the securities being offered hereby is being passed upon for us, by Skadden, Arps, Slate, Meagher & Flom LLP, Boston, Massachusetts.

**EXPERTS**

The audited financial statements incorporated in this prospectus by reference to the Annual Report on Form 10-K/A Amendment No. 2 of our company for the year ended December 31, 2003, except as they relate to Amgen-Regeneron Partners for the year ended December 31, 2001, have been audited by PricewaterhouseCoopers LLP, an independent registered public accounting firm, and insofar as they relate to Amgen-Regeneron Partners for the year ended December 31, 2001, by Ernst & Young LLP, independent auditors, whose reports thereon are incorporated by reference herein. Such financial statements have been so incorporated in reliance on the reports of such independent registered public accounting firm and independent auditors given on the authority of such firms as experts in auditing and accounting.

The financial statements of Amgen-Regeneron Partners appearing in Regeneron Pharmaceuticals, Inc.'s Annual Report (Form 10-K/A Amendment No. 2) for the year ended December 31, 2003, have been audited by Ernst & Young LLP, independent auditors, as set forth in their report thereon included therein and incorporated herein by reference. Such financial statements are incorporated herein in reliance upon the report of Ernst & Young LLP pertaining to such financial statements given on the authority of such firm as experts in accounting and auditing.

**Table of Contents****PART II****INFORMATION NOT REQUIRED IN PROSPECTUS****Item 14. *Other Expenses of Issuance and Distribution***

The following table sets forth our expenses in connection with the offerings described in this Registration Statement. All expenses, other than the SEC registration fee, are estimates.

SEC Registration Fee	\$ 23,540
Transfer Agents, Trustees and Depositary s Fees, and Expenses	\$ 50,000
Printing and Engraving Fees and Expenses	\$ 100,000
Accounting Fees and Expenses	\$ 500,000
Stock Exchange Listing Fees	\$ 50,000
Legal Fees	\$ 500,000
Rating Agency Fees	\$ 150,000
Miscellaneous	\$ 50,000
	<hr/>
Total	\$ 1,423,540

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

Article Seven of our Restated Certificate of Incorporation requires indemnification of our officers and directors and that such indemnification be made to the fullest extent permitted by the New York Business Corporation Law.

Section 722 of the New York Business Corporation Law permits a corporation to provide for the indemnification of the members of its board of directors and its officers against actions or proceedings, or the threat thereof, by or in the right of the corporation. In order to receive indemnification, such director or officer must have (i) acted in good faith for a purpose which he reasonably believed was in the best interest of the corporation, and (ii) in the case of a criminal proceeding, also had no reasonable belief that such conduct was unlawful.

Article IV of our By-Laws provides that the directors and certain other personnel of our company shall be indemnified against expenses and certain other liabilities arising out of legal actions brought or threatened against them for their conduct on behalf of our company, subject to certain qualifications and provided that each such person acted in good faith and in a manner that they reasonably believed was in our best interest.

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers or persons controlling us pursuant to the foregoing provisions or otherwise, we have been informed that in the opinion of the SEC such indemnification is against public policy as expressed in the Securities Act and is therefore unenforceable.

We have agreements with some of our directors which provide that we will indemnify them to the fullest extent permitted by the New York Business Corporation Law. We maintain directors and officers liability insurance which insures against liabilities that our directors or officers may incur in such capacities.

**Table of Contents****Item 16. Exhibits**

Exhibit No.	Description
1.1**	Form of underwriting agreement.
4.1	Restated Certificate of Incorporation of Regeneron Pharmaceuticals, Inc.(1)
4.2	Certificate of Amendment of the Certificate of Incorporation of Regeneron Pharmaceuticals, Inc.(2)
4.3	Certificate of Amendment of the Certification of Incorporation of Regeneron Pharmaceuticals, Inc.(3)
4.4	Bylaws of Regeneron Pharmaceuticals, Inc.(4)
4.5	Amendment to the Bylaws of Regeneron Pharmaceuticals, Inc.(5)
4.6	Form of indenture.
4.7**	Supplemental indenture or other instrument creating a series of debt securities under the indenture.
4.8**	Form of any debt security.
4.9**	Form of preferred stock.
4.10**	Form of any preferred stock certificate.
4.11**	Form of warrant agreement.
4.12**	Form of warrant certificate.
4.13	Rights Agreement, dated as of September 20, 1996, between Regeneron Pharmaceuticals, Inc. and Chase Mellon Shareholder Services LLC, as Rights Agent, including the form of Rights Certificate as Exhibit B thereto.(6)
4.14	Registration Rights Agreement, dated as of March 28, 2003, by and between Novartis Pharma AG and Regeneron Pharmaceuticals, Inc.(7)
4.15	Stock Purchase Agreement, dated as of September 5, 2003, by and between Aventis Pharmaceuticals Inc. and Regeneron Pharmaceuticals, Inc.(8)
4.16	Form of certificate of shares of common stock.
5.1	Opinion of Skadden, Arps, Slate, Meagher & Flom LLP as to the legality of the debt securities, common stock, preferred stock, and warrants.
8.1**	Opinion of counsel as to certain tax matters.
12.1*	Statement re: computation of ratios of earnings to combined fixed charges of Regeneron Pharmaceuticals, Inc.
23.1	Consent of PricewaterhouseCoopers LLP, Independent Registered Public Accounting Firm.
23.2	Consent of Ernst & Young LLP, Independent Auditors.
23.3	Consent of Skadden, Arps, Slate, Meagher & Flom LLP (included in Exhibit 5.1).
24.1*	Power of Attorney of certain officers and directors of Regeneron Pharmaceuticals, Inc.
25.1	Statement of Eligibility and Qualification of trustee under the Indenture for Regeneron Pharmaceuticals, Inc. (to be filed in accordance with the Undertaking set forth in Section 512(j) of Regulation S-K under the Securities Act of 1933, as

amended).

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\* Previously filed.

\*\* To be filed by amendment or as an exhibit to a document to be incorporated or deemed to be incorporated by reference in this Registration Statement.

- (1) Incorporated by reference from the Form 10-Q for Regeneron Pharmaceuticals, Inc. for the quarter ended June 30, 1991, filed August 13, 1991.
- (2) Incorporated by reference from the Form 10-Q for Regeneron Pharmaceuticals, Inc. for the quarter ended September 30, 1996, filed November 8, 1996.
- (3) Incorporated by reference from the Form 10-K for Regeneron Pharmaceuticals, Inc. for the fiscal year ended December 31, 2001, filed March 22, 2002.

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- (4) Incorporated by reference from the Form 10-K for Regeneron Pharmaceuticals, Inc. for the fiscal year ended December 31, 1994, filed March 30, 1995.
- (5) Incorporated by reference from the Form 8-K for Regeneron Pharmaceuticals, Inc. filed November 12, 2004.
- (6) Incorporated by reference from the Form 8-A for Regeneron Pharmaceuticals, Inc. filed October 15, 1996.
- (7) Incorporated by reference from the Form 10-Q for Regeneron Pharmaceuticals, Inc. for the quarter ended March 31, 2003, filed May 15, 2003.
- (8) Incorporated by reference from the Form 10-Q for Regeneron Pharmaceuticals, Inc. for the quarter ended September 30, 2003, filed November 12, 2003.

**Item 17. Undertakings**

(A) 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 of 1933;
  - (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 volume of 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 SEC pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than a 20 percentage change in the maximum aggregate offering price set forth in the Calculation of Registration Fee table in the effective registration statement.
  - (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 (1)(i) and 1(ii) do not apply if the information required to be included in a post-effective amendment by those paragraphs is contained in periodic reports filed with or furnished to the SEC by the registrant pursuant to Section 13 or Section 15(d) of the Securities Exchange Act that are incorporated by reference in the registration statement.
- (2) That, for the purpose of determining any liability under the Securities Act of 1933, 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.

(B) The undersigned registrants hereby undertake that, for purposes of determining any liability under the Securities Act of 1933, each filing of the registrant's annual report pursuant to Section 13(a) or Section 15(d) of the Exchange Act (and, where applicable, each filing of an employee benefit plan's annual report pursuant to 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 herein, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof.

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- (C) Insofar as indemnification for liabilities arising under the Securities Act of 1933 may be permitted to directors, officers and controlling persons of any of the registrants pursuant to the provisions set forth in Item 15, or otherwise, each of the registrants has been advised that in the opinion of the SEC such indemnification is against public policy as expressed in the Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by one of the registrants of expenses incurred or paid by a director, officer or controlling person of one of the registrants 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, each of the registrants 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 whether such indemnification by it is against public policy as expressed in the Act and will be governed by the final adjudication of such issue.
- (D) The undersigned registrant hereby undertakes to file an application for the purpose of determining the eligibility of the trustee to act under subsection (a) of Section 310 of the Trust Indenture Act in accordance with the rules and regulations prescribed by the Commission under Section 305(b)(2) of the Act.

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**SIGNATURES**

Pursuant to the requirements of the Securities Act of 1933, the registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on this Form S-3 and has duly caused this Registration Statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the Village of Tarrytown, State of New York, on this 9th day of February, 2005.

REGENERON PHARMACEUTICALS, INC.

By: /s/ MURRAY A. GOLDBERG

\_\_\_\_\_  
 Murray A. Goldberg  
*Senior Vice President, Finance & Administration*  
*Chief Financial Officer,*  
*Treasurer and Assistant Secretary*

**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 indicated on February 9, 2005.

/s/ LEONARD S. SCHLEIFER, M.D., PH.D. _____ Leonard S. Schleifer, M.D., Ph.D.	President, Chief Executive Officer and Director (Principal Executive Officer)
/s/ MURRAY A. GOLDBERG _____ Murray A. Goldberg	Senior Vice President, Finance & Administration, Chief Financial Officer, Treasurer and Assistant Secretary (Principal Financial Officer)
/s/ DOUGLAS S. MCCORKLE _____ Douglas S. McCorkle	Controller and Assistant Treasurer (Chief Accounting Officer)
* _____	Chairman of the Board
P. Roy Vagelos, M.D. * _____	Director
Charles A. Baker * _____	Director
Michael S. Brown, M.D. * _____	Director
Alfred G. Gilman, M.D. * _____	Director
Joseph L. Goldstein, M.D.	

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Director

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Arthur F. Ryan

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*	Director
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Eric M. Shooter, M.D.	
*	Director
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George L. Sing	
*	Director
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George D. Yancopoulos, M.D., Ph.D.	
*By: <u>          /s/ MURRAY A. GOLDBERG          </u>	Attorney-in-fact
Murray A. Goldberg	

**Table of Contents****EXHIBIT INDEX**

Exhibit No.	Description
1.1**	Form of underwriting agreement.
4.1	Restated Certificate of Incorporation of Regeneron Pharmaceuticals, Inc.(1)
4.2	Certificate of Amendment of the Certificate of Incorporation of Regeneron Pharmaceuticals, Inc.(2)
4.3	Certificate of Amendment of the Certification of Incorporation of Regeneron Pharmaceuticals, Inc.(3)
4.4	Bylaws of Regeneron Pharmaceuticals, Inc.(4)
4.5	Amendment to the Bylaws of Regeneron Pharmaceuticals, Inc.(5)
4.6	Form of indenture.
4.7**	Supplemental indenture or other instrument creating a series of debt securities under the indenture.
4.8**	Form of any debt security.
4.9**	Form of preferred stock.
4.10**	Form of any preferred stock certificate.
4.11**	Form of warrant agreement.
4.12**	Form of warrant certificate.
4.13	Rights Agreement, dated as of September 20, 1996, between Regeneron Pharmaceuticals, Inc. and Chase Mellon Shareholder Services LLC, as Rights Agent, including the form of Rights Certificate as Exhibit B thereto.(6)
4.14	Registration Rights Agreement, dated as of March 28, 2003, by and between Novartis Pharma AG and Regeneron Pharmaceuticals, Inc.(7)
4.15	Stock Purchase Agreement, dated as of September 5, 2003, by and between Aventis Pharmaceuticals Inc. and Regeneron Pharmaceuticals, Inc.(8)
4.16	Form of certificate of shares of common stock.
5.1	Opinion of Skadden, Arps, Slate, Meagher & Flom LLP as to the legality of the debt securities, common stock, preferred stock, and warrants.
8.1**	Opinion of counsel as to certain tax matters.
12.1*	Statement re: computation of ratios of earnings to combined fixed charges of Regeneron Pharmaceuticals, Inc.
23.1	Consent of PricewaterhouseCoopers LLP, Independent Registered Public Accounting Firm.
23.2	Consent of Ernst & Young LLP, Independent Auditors.
23.3	Consent of Skadden, Arps, Slate, Meagher & Flom LLP (included in Exhibit 5.1).
24.1*	Power of Attorney of certain officers and directors of Regeneron Pharmaceuticals, Inc.

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25.1 Statement of Eligibility and Qualification of trustee under the Indenture for Regeneron Pharmaceuticals, Inc. (to be filed in accordance with the Undertaking set forth in Section 512(j) of Regulation S-K under the Securities Act of 1933, as amended).

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\* Previously filed.

\*\* To be filed by amendment or as an exhibit to a document to be incorporated or deemed to be incorporated by reference in this Registration Statement.

- (1) Incorporated by reference from the Form 10-Q for Regeneron Pharmaceuticals, Inc. for the quarter ended June 30, 1991, filed August 13, 1991.
- (2) Incorporated by reference from the Form 10-Q for Regeneron Pharmaceuticals, Inc. for the quarter ended September 30, 1996, filed November 8, 1996.
- (3) Incorporated by reference from the Form 10-K for Regeneron Pharmaceuticals, Inc. for the fiscal year ended December 31, 2001, filed March 22, 2002.
- (4) Incorporated by reference from the Form 10-K for Regeneron Pharmaceuticals, Inc. for the fiscal year ended December 31, 1994, filed March 30, 1995.