EXACT SCIENCES CORP
Form 424B5
January 27, 2004

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The information in this preliminary prospectus supplement and the accompanying prospectus is not complete and may be changed. This preliminary prospectus supplement and the accompanying prospectus are not an offer to sell these securities and are not soliciting an offer to buy these securities in any state where the offer or sale is not permitted.

Subject to Completion
Preliminary Prospectus Supplement dated January 26, 2004

PROSPECTUS SUPPLEMENT
(To prospectus dated September 25, 2003)

6,000,000 Shares

EXACT SCIENCES CORPORATION

Common Stock

We are offering 6,000,000 shares of our common stock.

Our common stock is quoted on the Nasdaq National Market under the symbol "EXAS." On January 23, 2004, the last sale price of our common stock as reported on the Nasdaq National Market was $9.96 per share.

Investing in our common stock involves a high degree of risk that is described in the Risk Factors section beginning on page S-11 of this prospectus supplement.

	Per Share	Total
Public offering price	$	$
Underwriting discounts and commissions	$	$
Proceeds, before expenses, to EXACT Sciences Corporation	$	$

The underwriters may also purchase up to 900,000 additional shares of our common stock at the public offering price, less the underwriting discounts and commissions, within 30 days from the date of this prospectus supplement to cover overallotments. If the overallotment option is exercised in full, we will receive additional proceeds, before expenses, of $.

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

The shares will be ready for delivery on or about , 2004.

Joint Book-Running Managers

Merrill Lynch & Co. **UBS Investment Bank**

Thomas Weisel Partners LLC **Leerink Swann & Company**

The date of this prospectus supplement is , 2004.

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Prospectus Supplement

Prospectus

You should rely only on the information incorporated by reference or provided in this prospectus supplement and the accompanying prospectus. We have not, and the underwriters have not, authorized anyone else to provide you with information that is different. We are only offering the securities in states where it is legal to offer and sell them. You should not assume that the information in this prospectus supplement or the accompanying prospectus is accurate as of any date other than the date on the cover page of the documents. If any statement in one of these documents is inconsistent with a statement in another document having a later date for example, a document incorporated by reference in this prospectus supplement or the accompanying prospectus the statement in the document having the later date modifies or supersedes the earlier statement.

Important Notice About Information Presented in This

Prospectus Supplement and the Accompanying Prospectus

In this prospectus supplement and the accompanying prospectus, the terms "EXACT," "the Company," "we," "us" and "our" refer to EXACT Sciences Corporation and its subsidiary.

We provide information to you about our common stock in two separate documents: (a) the accompanying prospectus, which provides general information, and (b) this prospectus supplement, which describes the specific details regarding this offering. If information in this prospectus supplement is inconsistent with the prospectus, you should rely on this prospectus supplement.

You should also read and consider the information in the documents we have referred you to in "Where You Can Find More Information" on page S-29 of this prospectus supplement and "Incorporation By Reference" on page 23 of the accompanying prospectus. The information incorporated by reference is considered to be part of this prospectus supplement, and information that we file later with the SEC will automatically update and supersede this information.

Except as otherwise indicated, the information in this prospectus supplement assumes no exercise of the underwriters' overallotment option to purchase additional shares of common stock.

FORWARD-LOOKING STATEMENTS

This prospectus supplement and the accompanying prospectus (including any document incorporated by reference herein or therein) includes forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, or the Exchange Act, that are subject to the "safe harbor" created by those sections. Some of the forward-looking statements can be identified by the use of forward-looking terms such as "believes," "expects," "may," "will," "should," "could," "seek," "intends," "plans," "estimates," "anticipates" or other comparable terms. Forward-looking statements involve inherent risks and uncertainties, which are difficult to predict and many of which are beyond our control. A number of important factors could cause actual results to differ materially from those described in the forward-looking statements, including those factors discussed in "Risk Factors" in this prospectus supplement and in the documents incorporated by reference herein or in the accompanying prospectus. Factors that could cause actual results to differ from those reflected in forward-looking statements relating to our operations and business include:

- the failure to meet expectations with respect to our future performance;
- the success of our strategic relationship with LabCorp;
- our inability to license certain technologies or maintain our license agreements;
- our dependence on the outcome of clinical studies to prove the superiority of our products and services;
- reliance on third-party payors to provide adequate reimbursement;
- our dependence on third parties for the supply of raw materials and components;
- the failure of the PreGen-Plus test to be included within colorectal cancer screening guidelines;
- pricing pressures and other competitive factors;
- demand for and market acceptance of our products and services;

the successful development of products and services and the timing of product and service introductions;

the availability and extent of utilization of manufacturing capacity and raw materials;

failure to comply with U.S. Food and Drug Administration requirements or other governmental regulations;

our ability to protect our intellectual property;

our ability to develop and implement new technologies successfully;

our ability to attract and retain qualified personnel;

changes in healthcare policy;

the uncertainties of litigation; and

other risks and uncertainties, including those set forth or incorporated in this prospectus supplement and in the documents incorporated by reference herein and those detailed from time to time in our filings with the Securities and Exchange Commission.

You should read this prospectus supplement and the accompanying prospectus and the documents incorporated by reference herein and therein completely and with the understanding that actual future results may be materially different from expectations. All forward-looking statements made or incorporated by reference in this prospectus supplement are qualified by these cautionary statements. These forward-looking statements are made only as of the date of this prospectus supplement and we do not undertake any obligation, other than as may be required by law, to update or revise any forward-looking statements to reflect changes in assumptions, the occurrence of unanticipated events or changes in future operating results over time.

PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights information contained elsewhere in this prospectus supplement, the accompanying prospectus and the documents incorporated herein and therein. This summary does not contain all the information that you should consider before deciding to invest in our common stock. We urge you to read this entire prospectus supplement and the accompanying prospectus carefully, including the risk factors in this prospectus supplement, the accompanying prospectus and in the documents identified under "Where You Can Find More Information" in this prospectus supplement and under "Incorporation by Reference" in the accompanying prospectus.

Overview

We are an applied genomics company that develops and commercializes proprietary DNA-based tests for the early detection of cancer. Our first commercial test, PreGen-Plus , is used for screening colorectal cancer, the second leading cause of cancer death in the U.S. and the leading cause of cancer death among non-smokers. Each year, more than 50 million Americans over the age of 50 who should be screened annually for colorectal cancer fail to follow the American Cancer Society's screening guidelines. Of those people for whom screening is recommended, many reject the option of colonoscopy, which, while accurate as a means of detecting colorectal cancer, is invasive, requires unpleasant bowel preparation and involves risks of damaging the colon. Until the commercial launch of PreGen-Plus, the only non-invasive option for colorectal cancer detection had been fecal occult blood testing, or FOBT. FOBT, however, suffers from relatively low sensitivity, particularly in detecting the early stage, most curable cancers, and requires dietary modifications, unpleasant stool sampling and stool manipulation by the patient. With

the U.S. launch in August 2003 of PreGen-Plus, our first commercially-available DNA-based cancer screening test for the average risk population, these patients now have a more accurate, non-invasive screening option for colorectal cancer. PreGen-Plus has been clinically shown to be four times more sensitive in detecting colorectal cancer than the most commonly used FOBT screening test on the market today.

It is widely accepted in the medical community that colorectal cancer screening is strongly recommended and that colorectal cancer is highly curable if detected early. However, according to the American Cancer Society, each year, nearly 150,000 people are diagnosed with the illness and almost 60,000 people die from it. Many of these people die because they are not screened for colorectal cancer or they use ineffective screening methods that either fail to detect the cancer or detect it at a later stage, when the five-year survival rate falls below 50%. Moreover, the number of people who die annually from the disease has remained relatively unchanged over the last 20 years, despite the availability of multiple colorectal cancer screening options, all of which we believe fail to meet the collective needs of patients, doctors and payors.

Since our founding in 1995 we have worked to apply the scientific discoveries about the human genome to address the significant unmet clinical need for an accurate, non-invasive colorectal cancer screening test that could reduce mortality through early detection and increased patient compliance. With the knowledge that survival rates approach 90% for patients whose colorectal cancers are detected in their earliest stages, but with too few patients getting adequately screened, we targeted the development of a safe, simple, non-invasive test that could save more lives. Our goal was to design a test that would be both easy to use and demonstrably more effective than other options such as FOBT in detecting early-stage cancers in an average-risk, asymptomatic population.

These development efforts led to the creation of PreGen-Plus. Our test includes proprietary and patented technologies that isolate and analyze the trace amounts of human DNA that are shed into stool every day from the exfoliation of cells that line the colon. When colorectal cancer is present, a minute portion of the total isolated human DNA will represent DNA shed from cancerous or pre-cancerous lesions. Once the human DNA in the sample is isolated, PreGen-Plus identifies specific

mutations and other abnormalities in that DNA associated with colorectal cancer and pre-cancerous lesions.

We believe that no traditional screening method on the market today (or *non-traditional* screening methods, such as virtual colonoscopy and immunochemical FOBT) allows for the early and accurate detection of colorectal cancer in a manner that is acceptable to patients, medical practitioners and payors. We believe that because PreGen-Plus looks for the *threshold* indications of colorectal cancer at the molecular level (e.g., genetic changes in DNA) rather than the more traditional clinical manifestations of colorectal cancer (e.g., blood in stool, viewable polyps or identifiable lesions), it is a powerful screening tool for the detection of colorectal cancer at its earliest stages. We have conducted several clinical studies supporting the performance of PreGen-Plus, including a recent 5,500 patient multi-center study that showed the ability of the test to detect colorectal cancer in 57% of the cases that were in the earliest stages, more than four times the detection rate of the leading FOBT on the market today, to which it was compared. Given its ease of use when compared to more traditional colorectal cancer screening methods, we believe that, based on data collected from a subset of over 3,500 patients from our multi-center study, more people will use PreGen-Plus as their screening option and, as a result, patient compliance with screening will improve. Further, we believe that PreGen-Plus, over time, can help to substantially reduce colorectal cancer mortality, just as cervical cancer deaths have been substantially reduced through regular Pap smear testing.

In August 2003, we commercialized PreGen-Plus in the United States through our exclusive licensee and strategic partner, Laboratory Corporation of America® Holdings (LabCorp®). We chose LabCorp as our strategic commercial partner for two important reasons. The first was our shared strategic vision about the influence the molecular diagnostics industry is expected to have on the healthcare system, as well as LabCorp's stated strategic focus on novel genomics-based products that could drive critical organic growth for its business. The second reason was a function of LabCorp's national breadth and distribution capability. LabCorp is the second largest commercial laboratory in the country and processes over 300,000 patient specimens daily through its system of 36 primary laboratories and over 1,000 patient service centers across the U.S. Additionally, LabCorp employs an 800-person primary care-focused sales force that has been trained extensively to sell PreGen-Plus. We expect that this will allow us to broaden our distribution reach in North America and maximize our commercial opportunity. In an effort to increase physician orders and third-party payor reimbursement, we and LabCorp are working with the physician, payor and patient communities to demonstrate the practical advantages of PreGen-Plus, including its cost-effectiveness. Given that PreGen-Plus is a safe, simple, and non-invasive test that has demonstrated a superior ability to detect early stage colorectal cancer when compared with the current non-invasive standard, we believe that physicians will increasingly order the test for their average-risk patients over the age of 50.

PreGen-Plus is DNA-based and, therefore, its performance is not limited by the biology of cancer. Accordingly, we are able to continuously improve the performance characteristics of the test. Our applied research and development efforts are currently focused on increasing the ability of the PreGen-Plus test to detect colorectal cancers as well as pre-cancerous lesions. For example, in the recently launched commercial version of the test, we incorporated a new sample preparation technology called Effipure . Effipure increases the yield of DNA that can be isolated from a stool sample, resulting in improved sensitivity compared to the performance of earlier versions of the test. As PreGen-Plus is not currently

subject to the lengthy approval process of the U.S. Food and Drug Administration, or FDA, improvements to the test generally can be introduced to the market through LabCorp as they are developed. This advantage provides us the flexibility to commercialize the most advanced version of the test nearly as quickly as we can develop and validate it.

PreGen-Plus has several advantages that we believe will lead to increased patient compliance and decreased mortality. These advantages include:

High sensitivity. We believe that PreGen-Plus can lead to increased detection of colorectal cancer, including early stage cancers and pre-cancerous lesions. Based on our multi-center study data, PreGen-Plus demonstrated a sensitivity four times greater than the leading FOBT, currently the most common non-invasive screening method for colorectal cancer, and more than four times as effective as the leading FOBT in detecting cancer at its early stages, when survival rates approach 90%.

Non-invasive, painless and convenient testing. Unlike current invasive screening and diagnostic methods, PreGen-Plus requires no pre-examination preparation, invasive procedures or anesthesia, and a sample can be collected in the privacy of one's home.

Simplicity. PreGen-Plus requires no special bowel preparation, dietary restrictions, changes in medications, or manipulation of stool by the patient.

DNA-based test allows for continual and efficient improvements. Unlike FOBT, PreGen-Plus is a DNA-based test and therefore its performance is not limited by the biology of cancer. Accordingly, this allows our scientific team to continue to improve the performance characteristics of PreGen-Plus through future technical innovations.

Commercial Strategy

On June 26, 2002, we entered into a license agreement and long-term strategic alliance with LabCorp to commercialize PreGen-Plus. Since then we have been actively working with LabCorp to improve the performance characteristics of PreGen-Plus and its market acceptance through the incorporation of technical changes such as Effipure. In addition, the August 2003 commercial launch of PreGen-Plus enabled us and LabCorp to refocus our efforts on new sales and marketing initiatives to help stimulate demand for the test. We and LabCorp amended this license agreement on January 19, 2004 to, among other things, restructure certain product development milestones and increase the level of our collaboration on sales initiatives and test enhancements.

Pursuant to the license agreement, as amended, we agreed to license to LabCorp all U.S. and Canadian patents and patent applications owned or exclusively licensed by us relating to PreGen-Plus. The license with LabCorp is exclusive in the U.S. and Canada for a five-year period after the commercial launch of PreGen-Plus followed by a non-exclusive license for the life of the patents. In return for the license, LabCorp has agreed to pay us certain up-front and milestone payments, and a per-test royalty fee based on the reimbursed amount of each test ordered by a physician and processed in LabCorp's facilities. These per-test royalty fees are subject to a minimum dollar amount per test. LabCorp made an initial payment of $15 million to us upon the signing of the agreement in June 2002, and a second payment of $15 million in August 2003 upon the commercial launch of PreGen-Plus. In addition, pursuant to the amended agreement, we may be eligible for additional milestone payments from LabCorp totaling up to $45 million, of which a total of up to $15 million relates to certain clinical guideline acceptance and policy-level reimbursement approvals and a total of up to $30 million relates to the achievement of significant LabCorp revenue thresholds. As part of the agreement, in June 2002 we issued to LabCorp a warrant to purchase 1,000,000 shares of our common stock, exercisable for cash over a three-year period, at an exercise price of $16.09 per share.

In connection with the commercialization of PreGen-Plus, we have been developing and implementing a marketing and reimbursement strategy. We have built a strategic sales team of 11 highly skilled and experienced individuals to help strategically guide and support the 800-person LabCorp sales force on PreGen-Plus initiatives. Our reimbursement strategy consists primarily of educating large managed care organizations, large self-insured employers and large physician groups about the clinical benefits and cost-effectiveness of using PreGen-Plus. We believe that both the

anticipated publication of our multi-center study results in a peer-reviewed journal and our cost-effectiveness study results that were presented at the Digestive Disease Week conference in May 2003 will aid in our efforts to gain reimbursement for the test. Between commercial launch and

December 31, 2003, LabCorp received over 500 patient samples for testing from physicians across the country, billed insurers and received payment from numerous third-party payors. Furthermore, payors representing approximately 10 million covered lives have approved reimbursement of PreGen-Plus for their appropriate patients, including two large employer groups who have agreed to pay for PreGen-Plus for their employees.

Clinical Studies

Our DNA-based technologies, including PreGen-Plus, have been the subject of extensive research and clinical studies. In numerous studies to date, the performance of PreGen-Plus has been examined in thousands of tissue and stool samples. In addition to several smaller clinical studies designed to measure the sensitivity and specificity of PreGen-Plus in detecting colorectal cancer, the performance of PreGen-Plus was compared to FOBT in a multi-center clinical study that enrolled approximately 5,500 average-risk, asymptomatic patients from more than 80 sites across the United States. The study was designed to determine whether PreGen-Plus was clinically superior to Hemoccult II®, an FOBT that is currently the most widely used non-invasive colorectal cancer screening option. The primary endpoint of the clinical study demonstrated strong statistical significance, with a p-value of less than 0.001. Results from the study, which were presented in October 2003 at the American College of Gastroenterology's Annual Conference, indicated that PreGen-Plus was four times more sensitive than this FOBT in detecting colorectal cancer (52% for PreGen-Plus versus 13% for FOBT), and more than four times more sensitive in detecting colorectal cancer in its earliest, most curable stages (57% for PreGen-Plus versus 13% for FOBT). There was no difference in specificity between PreGen-Plus and this FOBT, with both tests demonstrating a specificity of approximately 95%.

Scientifically and clinically, study results provide validation for the technology and its use in clinical practice. Commercially, published clinical study results provide the information necessary for thought leaders to evaluate PreGen-Plus for inclusion into colorectal cancer screening guidelines. Guideline inclusion is important both to physicians and to payors, who frequently follow such guidelines in evaluating new technologies.

The first colorectal cancer screening guidelines promulgated in 1997 by the GI Consortium, which includes physicians from the American College of Gastroenterology and the American Gastroenterological Association, stated that future studies of new technologies did not themselves have to encompass a mortality endpoint, but instead should be compared to currently available technologies that had already proven such a benefit. We therefore designed our multi-center study with this in mind, believing that demonstration of superiority with statistical significance would satisfy the directive from the GI Consortium, and thus increase the likelihood that the PreGen-Plus test would be included as an option in colorectal cancer screening guidelines.

Results from our clinical studies that have been published are summarized in the table below. The results of these studies may not be directly comparable as these studies were conducted across a variety of patient populations and clinical settings and employed varying sample collection protocols. The multi-center study referenced above, as well as all of our published clinical studies to date, reflect the performance of our original, bead-based version of PreGen-Plus. The commercial test currently

available includes several technological improvements, including Effipure, which we believe enhances the overall performance of the test.

Published Study	Completed	Number of Cancer Patients	Sensitivity	Specificity*
Mayo Clinic I Pilot Study	1999	22	91%	93%
University of Nebraska	2002	16	69%	*
Kaiser Clinic	2002	52	63%	98%
Boston	2002	68	63%	*

* Specificity can only be derived in studies that include a certain number of individuals without cancer. The studies in the table without a specificity figure did not contain the requisite number of disease-free individuals.

In October 2001, Mayo Clinic initiated a clinical study of PreGen-Plus, which is ultimately intended to include approximately 4,000 patients and is designed to compare the results of PreGen-Plus with those of FOBT. Our role in this study is limited to sample processing. Based on our information to date, we expect Mayo Clinic to complete enrollment in this clinical study in 2005.

In addition, we have had numerous abstracts accepted for presentation at industry and scientific meetings and have published articles in peer-reviewed journals, including *Gastroenterology, The New England Journal of Medicine* and the *Journal of the National Cancer Institute*.

We expect that virtually all validations of PreGen-Plus technology improvements, including sensitivity improvements, will be based on internal research studies that take advantage of past empirical data and research results. With the results of our existing body of clinical data to date, we do not believe that additional, large, multi-year clinical studies will be necessary to achieve validations of our technology improvements in the future.

Research and Development

Our research and development efforts focus on developing multiple, DNA-based methodologies for the early detection of cancer and pre-cancerous lesions. Specifically, we are working on developing methods to automate and simplify the collection, preparation and analysis of samples to produce cost-effective commercial tests. Our research and development efforts for the near-term will focus almost exclusively on PreGen-Plus in the following areas:

Technical performance improvement. We continue to focus our research and development efforts on improving the sensitivity of PreGen-Plus for both invasive cancer and pre-cancerous lesions. We have demonstrated that increasing the yield and purity of human DNA extracted from a stool sample will result in an increase in the sensitivity of the test. The commercial version of PreGen-Plus that was launched in August 2003 incorporates Effipure, our new sample preparation technology, that results in a higher yield of DNA as compared to our first generation, bead-based test that was used in all of our published studies to date. We intend to continue development work to improve human DNA yield and purity from a sample, increase the sensitivity of the test using its current configuration, and develop new configurations of the test to optimize performance.

While our research efforts to date have focused on the detection of colorectal cancer, some of the new technologies that we are investigating may enable us to better detect pre-cancerous lesions, especially those that are most likely to progress to invasive colorectal cancer. As part of this effort, we have developed and are evaluating a new method for scanning regions of DNA at sites often associated with pre-cancerous lesion development.

Process improvement. We are undertaking efforts to automate and reduce the cost of the PreGen-Plus testing process by seeking to eliminate certain manual steps, reduce the use of expensive reagents and increase processing throughput. These efforts are intended to enable us to continue to offer LabCorp and future strategic partners the most sensitive, robust and low-cost genomics-based tests possible.

Extensions to other cancers. We believe our proprietary DNA Integrity Assay, or DIA®, may potentially be applicable to the detection of other cancers in addition to colorectal cancer. DIA is a non-gene-specific marker for the presence of cancer, as indicated by longer, less degraded strands of DNA. The presence of these longer strands of DNA is believed to be associated with escape from apoptosis (natural cell death), which itself is a hallmark of cancer. We have validated the DIA theory through a collaboration with a bioinformatics company using a virtual model of cancer, and we are now working with our collaborators on a pre-clinical model. In addition, several independent papers were recently published that support our observations around DIA. We intend to investigate the potential of DIA in other applications, including:

- early detection of other common cancers among average-risk individuals;
- individual monitoring of transitions from benign proliferative disorders, such as polyps, cysts and warts, to malignant tumors;
- intra-individual therapeutic monitoring; and
- post-therapy screening for disease recurrence.

We were incorporated in the State of Delaware on February 10, 1995. Our executive offices are located at 100 Campus Drive, Marlborough, Massachusetts 01752. Our telephone number is 508-683-1200. Our web address is www.exactsciences.com. We do not intend for the information contained in our web site to be incorporated by reference into any part of this prospectus supplement and accompanying prospectus.

SUMMARY FINANCIAL DATA

The following table presents our summary consolidated financial data. You should read this information together with our consolidated financial statements and the notes to those statements incorporated by reference in this prospectus supplement and the accompanying prospectus.

	Year Ended December 31,		
	2001	2002	2003
	(in thousands except per share data)		
Consolidated Statement of Operations:			
Revenues:			
License fees.	$ 51	$ 886	$ 2,871
Product royalty			8
Product revenue		11	22
Total revenues	51	897	2,901
Gross profit:			
License fees	51	886	2,871
Product royalty			7
Product revenue		2	1
Total gross profit	51	888	2,879
Operating expenses:			
Research and development	13,335	19,989	17,084
Selling, general and administrative	9,078	9,701	13,515
Stock-based compensation	3,788	2,043	1,118
Total operating expenses	26,201	31,733	31,717
Loss from operations.	(26,150)	(30,845)	(28,838)
Interest income	2,665	962	498
Net loss	$ (23,485)	$ (29,883)	$ (28,340)
Net loss per common share - basic and diluted:	$ (1.42)	$ (1.62)	$ (1.50)

	Year Ended December 31,		
Weighted average common shares outstanding: basic and diluted	16,487	18,433	18,911

	As of December 31, 2003	
	Actual	As adjusted[1]
Consolidated Balance Sheet Data (in thousands):		
Cash, cash equivalents and short-term investments	$ 27,807	$ 83,607
Net working capital	22,366	78,166
Total assets	34,681	90,481
Total liabilities	22,453	22,453
Stockholders' equity	12,228	68,028

(1) As adjusted to give effect to the issuance of 6,000,000 shares of our common stock in this offering at an estimated public offering price of $9.96 per share, net of the estimated underwriting discounts and our estimated offering expenses.

THE OFFERING

Common stock offered	6,000,000 shares
Shares outstanding after the offering	25,245,977 shares
Use of proceeds	We estimate our net proceeds from this offering will be approximately $55.8 million, after deducting underwriting discounts and commissions and our estimated offering expenses, or $64.2 million if the underwriters exercise their overallotment option in full. We will use the net proceeds from this offering for sales and marketing, research and development activities, working capital and other general corporate purposes. See "Use of Proceeds."
Risk factors	You should review and consider the risks discussed under "Risk Factors" and other information included in this prospectus supplement and the accompanying prospectus before deciding to invest in shares of our common stock.
Nasdaq National Market symbol	EXAS

The number of shares to be outstanding after the offering is based on 19,245,977 shares outstanding as of December 31, 2003, and excludes:

- 900,000 additional shares of common stock that the underwriters have a right to purchase from us within 30 days from the date of this prospectus supplement to cover overallotments;
- 3,591,603 shares of common stock issuable upon exercise of options outstanding as of December 31, 2003 at a weighted average exercise price of $7.48 per share;

997,988 shares of common stock issuable upon exercise of stock options or purchased under the Company's stock purchase plan reserved for issuance as of December 31, 2003; and

1,000,000 shares of common stock issuable upon exercise of an outstanding warrant at an exercise price of $16.09 per share.

RISK FACTORS

This offering involves a high degree of risk. You should carefully consider the risks described below and the other information in this prospectus supplement and the accompanying prospectus before deciding to invest in shares of our common stock. While these are the risks and uncertainties we believe are most important for you to consider, you should know that they are not the only risks or uncertainties facing us or which may adversely affect our business. If any of the following risks or uncertainties actually occur, our business, financial condition and operating results would likely suffer. In that event, the market price of our common stock could decline and you could lose all or part of your investment in our common stock.

RISKS RELATED TO OUR COMPANY

We may never successfully commercialize any of our products or services or become profitable.

We have incurred losses since we were formed. From our date of inception on February 10, 1995 through December 31, 2003, we have accumulated a total deficit of approximately $104.8 million. We expect that our losses will continue for the next several years as a result of continuing research and development expenses, as well as increased sales and marketing expenses. We cannot assure you that the revenue from any of our products or services will be sufficient to make us profitable.

Our ability to generate revenue substantially depends on the success of our strategic relationship with LabCorp.

We have a long-term, strategic alliance with LabCorp, under which we licensed to LabCorp certain of our technologies that are required for the commercialization of PreGen-Plus, a proprietary, non-invasive DNA-based screening test for the early detection of colorectal cancer in the average-risk population. The license to LabCorp is exclusive within the United States and Canada for a five-year term followed by a non-exclusive license for the life of the underlying patents. LabCorp has the ability to terminate this agreement for, among other things, a material breach by us. If LabCorp were to terminate the agreement, or fail to meet its obligations under the agreement, our revenues would be materially adversely affected and the commercialization of PreGen-Plus would be interrupted. Further, we cannot guarantee that we would be able to enter into a similar agreement to commercialize this technology. Moreover, if we do not achieve certain milestones, or LabCorp does not achieve certain revenue and performance thresholds within the time periods prescribed in the agreement, we may not fully realize the expected benefits of the agreement to us.

In January 2004, we and LabCorp amended our license agreement, to among other things, restructure certain product development milestones and increase the level of our collaboration on sales and product enhancement initiatives. Although this amendment does not change the $45 million total milestone payments that we are eligible to receive under the agreement, the amendment may delay or make it more difficult for us to fully realize these payments if LabCorp is unable to achieve significant revenue thresholds with respect to its sales of PreGen-Plus or we are unable to obtain clinical guideline acceptance and policy-level reimbursement approvals for PreGen-Plus. If we do not receive additional milestone payments under our agreement with LabCorp, we may be required to raise additional funds to continue the development and commercialization of our PreGen-Plus technologies. Moreover, we cannot assure you that this amendment will accomplish the long-term goals of either party. If one or more additional amendments to our agreement with LabCorp become necessary as a result of the continuing evolution of PreGen-Plus, developments in our relationship with LabCorp or otherwise, we cannot assure you that any such amendment could be entered into on more favorable terms, if at all. If we and LabCorp are unsuccessful in managing our strategic relationship, we would be required to enter into other strategic relationships for the commercialization of PreGen-Plus or commercialize the test ourselves. We cannot assure you that we would be able to license our technology to another

commercial laboratory or otherwise successfully commercialize the technology, and our failure to do either of the foregoing would materially and adversely affect our ability to generate revenues.

Because our revenue will be substantially dependent upon LabCorp's commercial sales of PreGen-Plus, we are actively working together with LabCorp on initiatives designed to promote our joint success with regard to PreGen-Plus. Such initiatives include the following:

- test validation, technology transfer and licensing;
- contracting with manufacturers and suppliers;
- physician education and demand;
- broad-based reimbursement initiatives;
- advocacy development; and
- sales force training.

If we are unsuccessful in our efforts with respect to one or more of the foregoing initiatives, our revenues could be materially adversely affected.

Our business would suffer if we are unable to license certain technologies or obtain raw materials or if certain of our licenses were terminated.

The current configuration of PreGen-Plus that we have commercialized with LabCorp requires access to certain technologies and supply of raw materials for which we, or LabCorp, have entered into certain licensing and supply agreements. While we believe that we, or LabCorp, entered into agreements for such technologies and raw materials on favorable terms and conditions, no assurances can be given that we, or LabCorp, will be able to maintain these relationships. Furthermore, the configuration of PreGen-Plus may require us, or LabCorp to enter into additional licenses with third parties for other technologies and raw materials, and there can be no assurance that we, or LabCorp, can obtain these technologies and raw materials on acceptable terms, or at all. Any such additional licenses may require us to pay royalties or other fees to third parties, which would have an adverse effect on our revenues or gross margin. While we believe such third parties will meet their contractual responsibilities under current and future agreements, there can be no assurance that this will be the case or that such future agreements will in fact be negotiated and entered into. There can be no assurance that any of our current contractual arrangements between us and third parties, us and LabCorp, or between our strategic partners and other third parties, will be continued, entered into, or not breached or terminated early, or that we or our strategic partners will be able to enter into any future relationships necessary to the commercial sale of PreGen-Plus or necessary to our realization of material revenues. This could require the PreGen-Plus test to be re-configured which could negatively impact its commercial sale and increase the costs associated with the PreGen-Plus test, which could have a material adverse effect on our revenues and gross margin, respectively.

If our clinical studies do not prove the superiority of PreGen-Plus, we may experience reluctance or refusal on the part of physicians to order, and third-party payors to pay for tests based on PreGen-Plus.

In the first quarter of 2003, we concluded patient enrollment in a multi-center clinical study of our PreGen-Plus technology that included approximately 5,500 asymptomatic, average-risk aged 50 and older patients from over 80 academic and community-based medical practices. The goal of this clinical study was to provide additional data supporting the superiority of tests utilizing our technology versus the most widely used brand of FOBT, Hemoccult II, in detecting colorectal cancer in this average-risk population. Although this study achieved its primary endpoint of showing that our original, bead-based version of PreGen-Plus was four times more sensitive than Hemoccult II, the point sensitivity from our

multi-center clinical study was lower than that seen in our previous research and clinical studies. Accordingly, despite the success of this study, we and LabCorp may experience reluctance or refusal on the part of third-party payors to pay for tests using our technologies which could slow the demand for the PreGen-Plus test and adversely and materially impact revenues and profitability and, as a result, we may experience a decrease in our stock price.

In October 2001, we signed a Clinical Trial Agreement with Mayo Clinic in which the bead-based version of our PreGen-Plus test was made the subject of an independent study by Mayo Clinic, for which Mayo Clinic received a $4.9 million grant from the National Cancer Institute of the National Institutes of Health. This three-year study is expected to include approximately 4,000 patients at average risk for developing colorectal cancer and, similar to our multi-center clinical study, is designed to compare the results of our bead-based technologies with those of the Hemoccult II and Hemoccult Sensa®, two brands of FOBT, common first-line colorectal cancer screening options. The results of the Mayo clinical study may not show that tests using our technologies are sufficiently superior to Hemoccult II and Hemoccult Sensa. In that event, we may experience reluctance or refusal on the part of physicians to order, and third-party payors to pay for tests using our technologies, which could slow the demand for, and successful commercialization of, the PreGen-Plus test.

If Medicare and other third-party payors, including managed care organizations, do not provide adequate reimbursement for PreGen-Plus, the commercial success of PreGen-Plus could be compromised.

Many physicians may decide not to order colorectal cancer screening tests using our technologies unless the tests are adequately reimbursed by third-party payors such as Medicare and covered by managed care organizations. There is significant uncertainty concerning third-party reimbursement for the use of any test incorporating new technology. Reimbursement by a third-party payor may depend on a number of factors, including a payor's determination that tests using our technologies are: sensitive for colorectal cancer; not experimental or investigational; medically necessary; appropriate for the specific patient; and are cost-effective. While we and LabCorp have had some success in obtaining reimbursement from third-party payors for tests performed, to date, LabCorp has not secured any broad-based policy-level reimbursement approval from Medicare or enough third-party payors to ensure the long-term commercial success of PreGen-Plus.

Reimbursement by Medicare will require a review that may be lengthy and which may be performed under the provisions of a National Coverage Decision process. The Federal Balanced Budget Act of 1997 provides for adding new technologies to the colorectal cancer screening benefit, such as ours, with such frequency and payment limits as the Secretary of Health and Human Services, or HHS, determines appropriate. We cannot guarantee that the Secretary of HHS will act to approve tests based on our technologies on a timely basis, or at all.

Since policy-level reimbursement approval is required from each private payor individually, seeking such approvals is a time-consuming and costly process. If we, or LabCorp, are unable to obtain adequate reimbursement approval from Medicare and private payors for PreGen-Plus as a benefit, or if the amount reimbursed is inadequate, our ability to generate revenue from our PreGen-Plus tests will be limited.

If our Effipure technology and our or LabCorp's other technological advancements do not increase the performance of the PreGen-Plus test, the demand for PreGen-Plus may be negatively impacted.

We continue to work to improve the performance characteristics of PreGen-Plus through technical innovations such as our Effipure technology. However, there can be no assurance that future generations of our PreGen-Plus test, or the commercial version of the PreGen-Plus test currently offered by LabCorp, which incorporates Effipure and other technology improvements, will have

significantly greater sensitivity that that of our original bead-based technology that was used in the multi-center study. We have conducted studies of the commercial version of PreGen-Plus, which includes our Effipure technology. These studies, which have consisted of cohorts from previously conducted clinical studies, including the multi-center study, have shown that the commercial version of the PreGen-Plus test, which includes Effipure, detected cancer in additional samples that the original bead-based PreGen-Plus version did not. Although this ability of the commercial version of PreGen-Plus to detect previously missed cancers has been a consistent outcome across all of our internal studies, the number of samples in each of these studies has been small and the ranges of sensitivity improvement with Effipure have been broad, thus making it difficult to definitively quantify the increase in sensitivity of the commercial test as compared to the original bead-based test. If future generations of our PreGen-Plus test, or the commercial version of the PreGen-Plus test, with Effipure, does not have significantly greater sensitivity than that of the original bead-based technology, we may never achieve the expected demand for tests using our technologies or such demand could be significantly reduced, either of which would have a material adverse effect on our revenues.

The long-term commercial success of PreGen-Plus may be jeopardized if we, or LabCorp, are not able to lower costs through automating and simplifying key operational processes.

Currently, colorectal cancer screening tests using our technologies are more expensive than FOBT because they are labor-intensive and use highly complex processes and expensive reagents. In order to make our technologies less costly and more commercially attractive, we or LabCorp will need to reduce the costs of tests using our technologies through significant automation of key operational processes and other cost savings procedures. If we or LabCorp fail to create and improve technologies that sufficiently reduce costs, LabCorp's sales of PreGen-Plus and, as a result, our revenues may be limited.

If we are unable to convince medical practitioners to order tests using our technologies, our revenue and profitability may be limited.

If we, or LabCorp, fail to convince medical practitioners to order tests using our technologies, we will not be able to create sufficient demand for tests using our technologies in sufficient volume for us to become profitable. We and LabCorp will need to make thought-leading gastroenterologists and primary care physicians aware of the benefits of tests using our technologies through published papers, presentations at scientific conferences, favorable results from our clinical studies and obtaining reimbursement from insurers. Our failure to be successful in these efforts would make it difficult for us, or LabCorp, to convince medical practitioners to order colorectal cancer screening tests using our technologies for their patients which could materially adversely affect our revenues.

If PreGen-Plus is not included in colorectal cancer screening guidelines, physicians may not order PreGen-Plus and payors may not authorize reimbursement for PreGen-Plus.

An important element to market acceptance of PreGen-Plus and the test's successful commercialization involves the inclusion of PreGen-Plus in colorectal cancer screening guidelines. Guideline inclusion is in large part dependent upon the data from our multi-center study being accepted by, and published in, peer-reviewed journals. There can be no assurance that a peer-reviewed journal will accept or publish our multi-center study data, nor can there be any assurance that PreGen-Plus will be included within colorectal cancer screening guidelines any time soon, if at all. In the event PreGen-Plus is not included within colorectal cancer screening guidelines, our revenues, profits and results of operations would likely be materially and negatively affected.

We may experience limits on our revenue and profitability if only a small number of people decide to be screened for colorectal cancer using our technologies.

Even if our technologies are superior to alternative colorectal cancer screening technologies, adequate third-party reimbursement is obtained and medical practitioners order tests using our technologies, only a small number of people may decide to be screened for colorectal cancer. Despite the availability of current colorectal cancer screening methods as well as the recommendations of the American Cancer Society that all Americans over the age of 50 be screened for colorectal cancer, most of these individuals decide not to complete a colorectal cancer screening test. If only a small portion of the population decides to utilize colorectal cancer screening tests using our technologies, we will, despite our efforts, experience limits on our revenue and profitability.

If we or our partners fail to comply with FDA requirements, we may be limited or restricted in our ability to market our products and services and may be subject to stringent penalties.

The FDA does not actively regulate laboratory tests that are developed and used by a laboratory to conduct in-house testing. The FDA does regulate specific reagents and certain components, some of which are used with our technologies and react with a biological substance including those designed to identify a specific DNA sequence or protein. For instance, a key component of our technologies includes our Effipure technology for the recovery of DNA from biological samples. The FDA's regulations provide that most such reagents, which the FDA refers to as analyte specific reagents, or ASRs, are exempt from the FDA's pre-market review requirements. We believe that ASRs that we provide currently fall within these exemptions. However, if the FDA were to decide to more actively regulate in-house developed laboratory tests, or significantly change the regulations for ASRs, commercial sales of PreGen-Plus and the sale of Effipure components to LabCorp could be delayed, halted or prevented. If the FDA were to view any of our or LabCorp's actions as non-compliant, it could initiate enforcement action, which could involve criminal or civil penalties. Moreover, while we believe that Effipure qualifies as an analyte specific reagent, and is therefore exempt from the FDA's pre-market review requirements, there can be no assurance that the FDA or other regulatory bodies will agree with our assessment and the commercialization of our products and services could be impacted by being delayed, halted or prevented altogether. Finally, any ASRs that we provide will be subject to a number of FDA requirements, including compliance with the FDA's Quality System Regulation, which establishes extensive regulations for quality assurance and control as well as manufacturing procedures. Failure to comply with these regulations could result in enforcement action for us, our partners, or our contract manufacturers. Adverse FDA action in any of these areas could significantly increase our expenses and limit our revenue and profitability.

We may be subject to substantial costs and liability or be prevented from selling our screening tests for cancer as a result of litigation or other proceedings relating to patent rights.

Third parties may assert infringement or other intellectual property claims against our licensors, our licensees, our suppliers, our strategic partners, or us. We pursue a patent strategy that we believe provides us with a competitive advantage in the early detection of colorectal cancer and is designed to maximize our patent protection against third parties in the U.S. and in foreign countries. We have filed patent applications that cover methods we have designed to detect colorectal cancer and other cancers, including our testing process. In order to protect or enforce our patent rights, we may have to initiate actions against third parties. Any actions regarding patents could be costly and time-consuming, and divert our management and key personnel from our business. Additionally, such actions could result in challenges to the validity or applicability of our patents. Because the U.S. Patent & Trademark Office maintains patent applications in secrecy until a patent application publishes or the patent is issued, others may have filed patent applications covering technology used by us or our partners. Additionally, there may be third-party patents, patent applications and other intellectual property relevant to our

technologies that may block or compete with our technologies. Even if third-party claims are without merit, defending a lawsuit may result in substantial expense to us and may divert the attention of management and key personnel. In addition, we cannot provide assurance that we would prevail in any of these suits or that the damages or other remedies, if any, awarded against us would not be substantial. Claims of intellectual property infringement may require that we, or our strategic partners, enter into royalty or license agreements with third parties that may not be available on acceptable terms, if at all. These claims may also result in injunctions against the further development and commercial sale of PreGen-Plus, which would have a material adverse effect on our business, financial condition and results of operations.

Also, patents and applications owned by us may become the subject of interference proceedings in the United States Patent and Trademark Office to determine priority of invention, which could result in substantial cost to us, as well as a possible adverse decision as to the priority of invention of the patent or patent application involved. An adverse decision in an interference proceeding may result in the loss of rights under a patent or patent application subject to such a proceeding.

Additionally, a third-party has asserted claims of patent infringement against certain entities that are anticipated suppliers of materials necessary to the PreGen-Plus test as it is currently configured. Although to date no legal proceedings have been initiated against us, if any third party, including the third party discussed above, is successful in challenging the supply of materials needed for the PreGen-Plus test as it is currently configured, commercialization of our technologies may be significantly delayed, sales of the PreGen-Plus test may become interrupted, and our revenue may become impacted.

If we are unable to protect our intellectual property effectively, we may be unable to prevent third parties from using our intellectual property, which would impair our competitive advantage.

We rely on patent protection as well as a combination of trademark, copyright and trade secret protection, and other contractual restrictions to protect our proprietary technologies, all of which provide limited protection and may not adequately protect our rights or permit us to gain or keep any competitive advantage. If we fail to protect our intellectual property, we will be unable to prevent third parties from using our technologies and they will be able to compete more effectively against us.

As of December 31, 2003, we have 30 issued patents and 29 pending patent applications in the United States and we also have 33 issued foreign patents and 98 pending foreign patent applications. We cannot assure you that any of our currently pending or future patent applications will result in issued patents, and we cannot predict how long it will take for such patents to be issued. Further, we cannot assure you that other parties will not challenge any patents issued to us, or that courts or regulatory agencies will hold our patents to be valid or enforceable. A third-party institution is a co-owner of one of our issued patents relating to pooling patient samples in connection with our loss of heterozygosity detection method. We cannot guarantee you that we will be successful in defending challenges made in connection with our patents and patent applications. Any successful third-party challenge to our patents could result in co-ownership of such patents with a third party or the unenforceability or invalidity of such patents. In addition, we and a third-party institution have filed a joint patent application that is co-owned by us and that third-party institution relating to the use of various DNA markers, including one of our detection methods, to detect cancers of the lung, pancreas, esophagus, stomach, small intestine, bile duct, naso-pharyngeal, liver and gall bladder in stool under the Patent Cooperation Treaty. This patent application designates the United States, Japan, Europe and Canada. Co-ownership of a patent allows the co-owner to exercise all rights of ownership, including the right to use, transfer and license the rights protected by the applicable patent.

In addition to our patents, we rely on contractual restrictions to protect our proprietary technology. We require our employees and third parties to sign confidentiality agreements and

employees to sign agreements assigning to us all intellectual property arising from their work for us. Nevertheless, we cannot guarantee that these measures will be effective in protecting our intellectual property rights.

We cannot guarantee that the patents issued to us will be broad enough to provide any meaningful protection nor can we assure you that one of our competitors may not develop more effective technologies, designs or methods to test for colorectal cancer or any other common cancer without infringing our intellectual property rights or that one of our competitors might not design around our proprietary technologies.

If we become subject to additional regulations from the U.S. Department of Transportation, or other domestic and international regulatory agencies, for the transport of diagnostic specimens, it could increase the cost of transporting stool specimens and limit revenue growth.

On August 14, 2002, the U.S. Department of Transportation, or DOT, issued revised Hazardous Materials Regulations for the packaging and transport of infectious materials, including diagnostic specimens. In anticipation of the application of these regulations to our current specimen container and transport system, we submitted an exemption request to the DOT to minimize the changes that would be necessary for our specimen collection system, while still providing an equivalent level of safety. On February 13, 2003, the DOT issued a formal determination that stool samples intended for clinical research or diagnostic purposes would not be deemed an infectious substance subject to the Hazardous Materials Regulations. While this decision is favorable, we cannot be certain that the DOT, or other domestic and international regulatory agencies, will not more actively regulate or restrict the transportation of stool samples, such as those used in our diagnostic tests.

Other companies may develop and market novel or improved methods for detecting colorectal cancer, which may make our technologies less competitive, or even obsolete.

The market for colorectal cancer screening is large, approximating 80 million Americans age 50 and above, of which over 50 million fail to follow the American Cancer Society's screening guidelines. As a result, the colorectal screening market has attracted competitors, some of which have significantly greater resources than we have. Currently, we face competition from procedure-based detection technologies such as flexible sigmoidoscopy, colonoscopy and virtual colonoscopy, a new procedure being performed in which a radiologist views the inside of the colon through a scanner, as well as existing and possibly improved traditional screening tests such as immunochemical FOBT. In addition, some competitors are developing serum-based tests, or screening tests based on the detection of proteins or nucleic acids produced by colon cancer in the blood. These and other companies may also be working on additional methods of detecting colon cancer that have not yet been announced. We may be unable to compete effectively against these competitors either because their test is superior or because they may have more expertise, experience, financial resources and stronger business relationships.

We rely on third-party contract manufacturers and suppliers and may experience a scarcity of raw materials and components.

We rely on contract manufacturers and suppliers for certain components for our technologies. We believe that there are relatively few manufacturers that are currently capable of supplying commercial quantities of the raw materials and components necessary for the current configuration of the PreGen-Plus test, including our Effipure technology. Although we have identified suppliers that we believe are capable of supplying these raw materials and components in sufficient quantity today, there can be no assurance that we, or LabCorp, will be able to enter into agreements with such suppliers on a timely basis on acceptable terms, if at all. Furthermore, prior to August 2003, PreGen-Plus had never been offered on a commercial scale, and there can be no assurance that the raw materials and

components necessary to meet demand will be available in sufficient quantities or on acceptable terms, if at all. If we, or LabCorp, should encounter delays or difficulties in securing the necessary raw materials and components for PreGen-Plus, we may need to reconfigure the PreGen-Plus test which would result in delays in commercialization or an interruption in sales which could materially adversely impact our revenues.

The failure of LabCorp or any other laboratory using PreGen-Plus to comply with regulations governing clinical laboratories would materially adversely affect our business.

LabCorp and any other laboratory that uses PreGen-Plus is subject to the Clinical Laboratory Improvement Amendments of 1988, or CLIA. CLIA is a federal law which regulates clinical laboratories that perform testing on specimens derived from humans for the purpose of providing information for the diagnosis, prevention or treatment of disease. CLIA is intended to ensure the quality and reliability of clinical laboratories in the U.S. by mandating specific standards in the areas of personnel qualifications, administration, participation in proficiency testing, patient test management, quality control, quality assurance and inspections. If LabCorp were to lose its CLIA certification, it may no longer be able to offer PreGen-Plus, which would have a materially adverse effect on our business.

The loss of key members of our senior management team could adversely affect our business.

Our success depends largely on the skills, experience and performance of key members of our senior management team, including Don M. Hardison, our President and Chief Executive Officer, John A. McCarthy, Jr., our Executive Vice President, Chief Financial Officer and Treasurer, and Anthony P. Shuber, our Executive Vice President and Chief Technology Officer. Anthony P. Shuber has been critical to the development of our technologies and business. Although Messrs. Hardison, McCarthy and Shuber have each signed a non-disclosure and assignment of intellectual property agreement and a non-compete agreement, they have no employment agreements currently in place. We also have a severance agreement with each of Messrs. Hardison, McCarthy and Shuber that provides for twelve months severance under certain circumstances. The efforts of each of these persons will be critical to us as we continue to develop our technologies and testing processes and as we transition to a company with commercialized products and services. If we were to lose one or more of these key employees, we may experience difficulties in competing effectively, developing our technologies and implementing our business strategies.

If we lose the support of our key scientific collaborators, it may be difficult to establish tests using our technologies as a standard of care for colorectal cancer screening, which may limit our revenue growth and profitability.

We have established relationships with leading scientists, including members of our scientific advisory board, and research and academic institutions, such as Mayo Clinic and John Hopkins University, that we believe are key to establishing tests using our technologies as a standard of care for colorectal cancer screening. If our collaborators determine that colorectal cancer screening tests using our technologies are not superior to available colorectal cancer screening tests or that alternative technologies would be more effective in the early detection of colorectal cancer, we would encounter significant difficulty establishing tests using our technologies as a standard of care for colorectal cancer screening, which would limit our revenue growth and profitability.

Our inability to apply our proprietary technologies successfully to detect other common cancers may limit our revenue growth and profitability.

While, to date, we have focused substantially all of our research and development efforts on colorectal cancer, we have used our technologies to detect cancers of the lung, pancreas, esophagus, stomach and gall bladder. In the future, we intend to evaluate and potentially extend our technology

platform to the development of screening tests for these common cancers. To do so, we may need to overcome technological challenges to develop reliable screening tests for these cancers. There can be no assurance that our technologies will be capable of reliably detecting cancers, beyond colorectal cancer, with the sensitivity and specificity necessary to be clinically and commercially useful for such other cancers, or that we can develop such technologies at all. We may never realize any benefits from our research and development activities.

We may not have the ability to support demand.

The demand for the PreGen-Plus test may require us and LabCorp to implement certain increases in scale and related manufacturing and process improvements, and to establish an internal quality assurance program to support commercial testing. No assurance can be given that these increases in scale, related improvements and quality assurance program will be successfully implemented, and failure to do so could result in higher cost of testing or an inability to meet market demand. Since PreGen-Plus was recently introduced commercially in August 2003, there can be no assurance that LabCorp will be able to perform tests on a timely basis at a level consistent with demand. If LabCorp encounters difficulty meeting market demand for PreGen-Plus, there could be substantial interruption in LabCorp's continued ability to offer PreGen-Plus commercially and our revenue could be materially and adversely affected.

Changes in healthcare policy could subject us to additional regulatory requirements that may interrupt commercialization of the PreGen-Plus test and increase our costs.

Healthcare policy has been a subject of extensive discussion in the executive and legislative branches of the federal and many state governments. We developed our commercialization strategy for PreGen-Plus based on existing healthcare policies. Changes in healthcare policy could substantially interrupt the sales of PreGen-Plus, increase costs, and divert management's attention. We cannot predict what changes, if any, will be proposed or adopted or the effect that such proposals or adoption may have on our business, financial condition and results of operations.

Our inability to raise additional capital on acceptable terms in the future may limit our growth.

If our capital resources become insufficient to meet future requirements, we will have to raise additional funds to continue the development and commercialization of our technologies. Our inability to raise capital would seriously harm our business and development efforts. In addition, we may choose to raise additional capital due to market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operations. These funds may not be available on favorable terms, or at all. If adequate funds are not available on attractive terms, we may have to restrict our operations significantly or obtain funds by entering into agreements on unattractive terms. Further, to the extent that additional capital is raised through the sale of equity or convertible debt securities, the issuance of these securities could result in dilution to our stockholders.

Product liability suits against us could result in expensive and time-consuming litigation, payment of substantial damages and increases in our insurance rates.

The sale and use of our test could lead to the filing of product liability claims if someone were to allege that one of our products contained a design or manufacturing defect which resulted in the failure to detect the disease for which it was designed. A product liability claim could result in substantial damages and be costly and time consuming to defend, either of which could materially harm our business or financial condition. We cannot assure you that our product liability insurance would protect our assets from the financial impact of defending a product liability claim. Any product liability claim brought against us, with or without merit, could increase our product liability insurance rates or prevent us from securing insurance coverage in the future.

Our former independent public accountants, Arthur Andersen LLP, were found guilty of federal obstruction of justice charges, and you are unlikely to be able to exercise effective remedies against it in any legal action.

Prior to July 17, 2002, Arthur Andersen LLP served as the Company's independent auditors. On March 14, 2002, Arthur Andersen was indicted on federal obstruction of justice charges arising from the government's investigation of Enron Corporation and on June 15, 2002, Arthur Andersen was found guilty. Arthur Andersen informed the SEC that it would cease practicing before the SEC by August 31, 2002, unless the SEC determined that another date was appropriate. On May 7, 2002, the Company dismissed Arthur Andersen and retained Ernst & Young LLP as its independent auditors for its fiscal year ended December 31, 2002. SEC rules require the Company to present historical audited financial statements in various SEC filings, such as registration statements, along with Arthur Andersen's consent to the Company's inclusion of Arthur Andersen's audit report in those filings. Since the Company's former engagement partner and audit manager have left Arthur Andersen and in light of the cessation of Arthur Andersen's SEC practice, the Company is not able to obtain the consent of Arthur Andersen to the inclusion of Arthur Andersen's audit report in the Company's relevant current and future filings. The SEC has provided regulatory relief designed to allow companies that file reports with the SEC to dispense with the requirement to file a consent of Arthur Andersen in certain circumstances, but purchasers of securities sold under the Company's registration statements, which were not filed with the consent of Arthur Andersen to the inclusion of Arthur Andersen's audit report, will not be able to sue Arthur Andersen pursuant to Section 11(a)(4) of the Securities Act and therefore the purchasers' right of recovery under that section may be limited as a result of the lack of the Company's ability to obtain Arthur Andersen's consent.

Certain provisions of our charter, by-laws and Delaware law may make it difficult for you to change our management and may also make a takeover difficult.

Our corporate documents and Delaware law contain provisions that limit the ability of stockholders to change our management and may also enable our management to resist a takeover. These provisions include a staggered board of directors, limitations on persons authorized to call a special meeting of stockholders and advance notice procedures required for stockholders to make nominations of candidates for election as directors or to bring matters before an annual meeting of stockholders. These provisions might discourage, delay or prevent a change of control or in our management. These provisions could also discourage proxy contests and make it more difficult for you and other stockholders to elect directors and cause us to take other corporate actions. In addition, the existence of these provisions, together with Delaware law, might hinder or delay an attempted takeover other than through negotiations with our board of directors.

RISKS RELATED TO OUR COMMON STOCK

Our stock price may be volatile.

The market price of our common stock has fluctuated widely. For example, between September 10, 2003 and December 19, 2003, the closing price of our common stock dropped from approximately $17.55 to $8.85 per share and from March 3, 2003 to July 31, 2003 the price of our common stock rose from $8.35 to $17.11 per share. Consequently, the current market price of our common stock may not be indicative of future market prices and we may be unable to sustain or increase the value of an investment in our common stock. Factors affecting our stock price may include:

technological innovations or new products and services by us or our competitors;

clinical trial results relating to the PreGen-Plus tests or those of our competitors;

reimbursement decisions by Medicare and other third party payors;

FDA regulation of our products and services;

the establishment of collaborative partnerships;

health care legislation;

intellectual property disputes and other litigation;

additions or departures of key personnel;

the performance characteristics of our technologies;

general market conditions;

slow market acceptance of PreGen-Plus; and

sales of our common stock or debt securities.

Because we are a company with no significant operating revenue, you may consider one of these factors to be material.

Future sales by our existing stockholders could depress the market price of our common stock.

If our existing stockholders sell a large number of shares of our common stock, the market price of our common stock could decline significantly. Moreover, the perception in the public market that our existing stockholders might sell shares of common stock could adversely affect the market price of our common stock.

Our operating results may fluctuate, which may adversely affect our share price.

Fluctuations in our operating results may lead to fluctuations, including declines, in our share price. Our operating results may fluctuate from period to period due to a variety of factors, including:

demand by physicians and consumers for PreGen-Plus;

new technology introductions;

reimbursement acceptance success;

changes in our agreement with LabCorp;

the number and timing of milestones that we achieve under collaborative agreements;

the level of our development activity conducted for, and our success in commercializing these developments; and

the level of our spending on PreGen-Plus commercialization efforts, licensing and acquisition initiatives, clinical studies, and internal research and development.

Variations in the timing of our future revenue and expenses could also cause significant fluctuations in our operating results from period to period and may result in unanticipated earning shortfalls or losses. In addition, the Nasdaq National Market in general, and the market for biotechnology companies in particular, have experienced significant price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of those companies.

We may allocate net proceeds from this offering in ways with which you may not agree.

Our management will have broad discretion in using the proceeds from this offering and may allocate the use of the proceeds in ways with which you may disagree. Because we are not required to allocate the net proceeds form this offering to any specific investment or transaction, you cannot determine at this time the value or propriety of our application of the proceeds. Moreover, you will not have the opportunity to evaluate the economic, financial, or other information on which we base our decisions on how to use our proceeds. We may use the proceeds for corporate purposes that do not immediately enhance our prospects for the future or increase the value of your investment. As a result, you and other shareholders may not agree with our decisions.

USE OF PROCEEDS

We estimate that the net proceeds to us from the sale of the 6,000,000 shares of common stock we are offering will be approximately $55.8 million. If the underwriters fully exercise the overallotment option, the net proceeds to us will be approximately $64.2 million. For the purpose of estimating net proceeds, we are assuming that the public offering price will be $9.96 per share. "Net proceeds" is what we expect to receive after we pay the underwriting discounts and other estimated expenses for this offering.

We expect to use the net proceeds from the sale of these securities for general corporate purposes, including sales and marketing, and research and development. We may also use a portion of the net proceeds to acquire additional businesses, products and technologies, or to establish strategic alliances that we believe will complement our current or future business. We currently have no commitments or agreements with respect to any material transaction.

We will retain broad discretion in the allocation of the net proceeds of this offering. Pending the uses described above, we intend to invest the net proceeds of this offering in short-term interest-bearing securities. We cannot predict whether the proceeds will be invested to yield a favorable return.

PRICE RANGE OF COMMON STOCK AND DIVIDEND POLICY

Our common stock is listed on The Nasdaq National Market under the symbol "EXAS." The following table provides, for the periods indicated, the high and low sales prices per share as reported by The Nasdaq National Market.

	High	Low
2004		
First quarter through January 23, 2004	$ 10.49	$ 9.46
2003		
First quarter	$ 12.17	$ 6.30
Second quarter	15.10	8.87
Third quarter	18.00	10.65
Fourth quarter	16.00	8.50
2002		
First quarter	$ 12.16	$ 7.27
Second quarter	17.40	9.32
Third quarter	15.90	9.75
Fourth quarter	15.99	9.65

On January 23, 2004, the last sale price reported on The Nasdaq National Market for our common stock was $9.96 per share. As of December 31, 2003, there were approximately 19,245,977 shares of our common stock outstanding held by approximately 100 holders of record.

We have never paid any cash dividends on our capital stock and do not plan to pay any cash dividends in the foreseeable future. Our current policy is to retain all of our earnings to finance future growth.

CAPITALIZATION

The following table presents our capitalization at December 31, 2003:

- on an actual basis; and
- on an as adjusted basis to give effect to the issuance of 6,000,000 shares of our common stock in this offering at an estimated public offering price of $9.96 per share, net of the estimated underwriting discount and our estimated offering expenses.

The number of shares of common stock to be outstanding after this offering does not include:

- 900,000 additional shares of common stock that the underwriters have a right to purchase from us within 30 days from the date of this prospectus supplement to cover overallotments;
- 3,591,603 shares of common stock issuable upon exercise of options outstanding as of December 31, 2003 at a weighted average exercise price of $7.48 per share;
- 997,988 shares of common stock issuable upon exercise of stock options or purchased under the Company's stock purchase plan reserved for issuance as of December 31, 2003; and
- 1,000,000 shares of common stock issuable upon exercise of an outstanding warrant at an exercise price of $16.09 per share.

This table should be read with "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our financial statements and the accompanying notes set forth in our most recent quarterly and annual reports and incorporated herein by reference.

	As of December 31, 2003	
	Actual	As Adjusted
		(unaudited)
Cash, cash equivalents and short and long-term marketable securities	$ 27,807	$ 83,607
Long-term debt (including current portion)		
Stockholders' equity:		
Common stock, $0.01 par value, 100,000,000 authorized; 19,306,936 shares issued and outstanding, actual; 25,306,936 shares issued and outstanding, as adjusted	193	253
Additional paid-in capital	118,225	173,965
Deferred compensation	(729)	(729)
Treasury stock	(12)	(12)
Notes receivable	(641)	(641)
Unrealized loss on marketable securities	(1)	(1)
Accumulated deficit	(104,807)	(104,807)
Total stockholders' equity 12,228	68,028	
Total capitalization	12,228	68,028

DILUTION

If you invest in our common stock, your interest would be diluted to the extent of the difference between the public offering price per share of our common stock set forth on the cover page of this prospectus supplement and the adjusted net tangible book value per share of our common stock after this offering. Our reported net tangible book value per share as of December 31, 2003 is $0.50. We calculate net tangible book value per share by dividing net tangible book value, which equals total tangible assets less total tangible liabilities, by the number of outstanding shares of our common stock.

At the assumed public offering price of $9.96 per share, our as adjusted net tangible book value at December 31, 2003 would have been $2.59 per share. This represents an immediate increase in the net tangible book value per share of $2.09 per share to existing stockholders and an immediate dilution of $7.37 per share to new investors purchasing shares of common stock in this offering.

The following table illustrates this dilution on a per share basis:

Assumed public offering price per share		$ 9.96
Reported net tangible book value per share as of December 31, 2003	$ 0.50	
Increase per share attributable to new investors	$ 2.09	
As adjusted net tangible book value per share after this offering		
Dilution per share to new investors		$ 2.59

To the extent that outstanding options are exercised, there may be further dilution to new investors.

UNDERWRITING

We and the underwriters for this offering named below have entered into an underwriting agreement concerning the common stock being offered. Subject to conditions, each underwriter has severally agreed to purchase the number of shares indicated in the following table. Merrill Lynch, Pierce, Fenner & Smith Incorporated and UBS Securities LLC are the joint book-running managers of this offering and are acting as the representatives of the underwriters.

Underwriter	Number of Shares
Merrill Lynch, Pierce, Fenner & Smith Incorporated	
UBS Securities LLC	
Thomas Weisel Partners LLC	
Leerink Swann & Company	
Total	6,000,000

The underwriters have agreed to purchase all of the shares sold under the underwriting agreement if any of these shares are purchased. If an underwriter defaults, the underwriting agreement provides that the purchase commitments of the non-defaulting underwriters may be increased or the underwriting agreement may be terminated.

We have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act, or to contribute to payments the underwriters may be required to make in respect of those liabilities.

The underwriters are offering the shares, subject to prior sale, when, as and if issued to and accepted by them, subject to approval of legal matters by their counsel, including the validity of the shares, and other conditions contained in the underwriting agreement, such as the receipt by the underwriters of officer's certificates and legal opinions. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

Commissions and Discounts

The representatives have advised us that the underwriters propose initially to offer the shares to the public at the public offering price on the cover page of this prospectus supplement and to dealers at that price less a concession not in excess of $ per share. The underwriters may allow, and the dealers may reallow, a discount not in excess of $ per share to other dealers. After the offering, the public offering price, concession and discount may be changed.

The following table shows the public offering price, underwriting discount and proceeds before expenses to us. The information assumes either no exercise or full exercise by the underwriters of their overallotment option.

	Per Share	Without Option	With Option
Public offering price	$	$	$
Underwriting discount	$	$	$
Proceeds, before expenses, to EXACT Sciences Corporation	$	$	$

The expenses of the offering, not including the underwriting discount, are estimated at approximately $375,000 and are payable by us.

Overallotment Option

We have granted an option to the underwriters to purchase up to 900,000 additional shares at the public offering price less the underwriting discount. The underwriters may exercise this option for 30 days from the date of this prospectus supplement solely to cover any overallotments. If the underwriters exercise this option, each will be obligated, subject to conditions contained in the underwriting agreement, to purchase a number of additional shares proportionate to that underwriter's initial amount reflected in the above table.

No Sale of Similar Securities

We, our directors and our executive officers have agreed, with certain exceptions, not to sell or transfer any common stock for 90 days after the date of this prospectus supplement without first obtaining the consent of Merrill Lynch and UBS Securities LLC. Specifically, these directors and officers have agreed not to directly or indirectly:

offer, pledge, sell, or contract to sell any common stock;

sell any option or contract to purchase any common stock;

purchase any option or contract to sell any common stock;

grant any option, right or warrant for the sale of any common stock;

otherwise dispose of or transfer any common stock;

file, or cause to be filed, any registration statement under the Securities Act of 1933, as amended, with respect to any common stock; or

enter into any swap or any other agreement or any transaction that transfers, in whole or in part, directly or indirectly, the economic consequence of ownership of any common stock, whether any such swap or transaction is to be settled by delivery of common stock or other securities, in cash or otherwise.

This lockup provision applies both to common stock and to any securities convertible into or exchangeable or exercisable for common stock.

Quotation on the Nasdaq National Market

Our shares of common stock are traded on the Nasdaq National Market under the symbol "EXAS."

Price Stabilization, Short Positions and Penalty Bids

Until the distribution of our common stock offered hereby is completed, the SEC rules may limit the underwriters from bidding for or purchasing our common stock. However, the representatives may engage in transactions that stabilize the price of our common stock, such as bids or purchases that peg, fix or maintain that price.

The underwriters may purchase and sell our common stock in the open market. These transactions may include short sales, stabilizing transactions and purchases to cover positions created by short sales. Short sales involve the sale by the underwriters of a greater number of shares than they are required to purchase in the offering.

"Covered" short sales are sales made in an amount not greater than the underwriters' option to purchase additional shares from us in the offering. The underwriters may close out any covered short position by either exercising their option to purchase additional shares or purchasing shares in the open market. In determining the source of shares to close out the covered short position, the underwriters

will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase shares through the overallotment option. "Naked" short sales are any sales in excess of such option. The underwriters must close out any naked short position by purchasing stock in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of our common stock in the open market after pricing that could adversely affect investors who purchase in the offering. Stabilizing transactions consist of various bids for or purchases of common stock made by the underwriters in the open market.

Similar to other purchase transactions, the underwriters' purchases to cover the syndicate short sales may have the effect of raising or maintaining the market price of our common stock or preventing or retarding a decline in the market price of our common stock. As a result, the price of our common stock may be higher than the price that might otherwise exist in the open market.

Neither we nor any of the underwriters make any representation or prediction as to the direction or magnitude of any effect that the transactions described above may have on the price of the common stock. In addition, neither we nor the underwriters make any representation that the underwriters will engage in these transactions or that these transactions, once commenced, will not be discontinued without notice.

Passive Market Making

In connection with this offering, underwriters and selling group members may engage in passive market making transactions in our common stock on the Nasdaq National Market in accordance with Rule 103 of Regulation M under the Exchange Act during a period before the commencement of offers or sales of our common stock and extending through completion of the distribution. A passive market maker must display its bid at a price not in excess of the highest independent bid of that security. However, if all independent bids are lowered below the passive market maker's bid, that bid must then be lowered when specified purchase limits are exceeded.

Electronic Distribution

The underwriters will be facilitating Internet distribution for this offering to certain of their Internet subscription customers. The underwriters intend to allocate a limited number of shares for sale to their online brokerage customers. Any such allocation for online distributions will be made on the same basis as other allocations. In connection with this offering, certain of the underwriters or securities dealers may distribute the prospectus and prospectus supplement electronically.

Other Relationships

Some of the underwriters and their affiliates have engaged in, and may in the future engage in, investment banking and other commercial dealings in the ordinary course of business with us. They have received customary fees and commissions for these previous transactions.

LEGAL MATTERS

The validity of the securities offered hereby will be passed upon for us by Testa, Hurwitz & Thibeault, LLP, Boston, Massachusetts. Certain legal matters in connection with the securities offered hereby will be passed upon for the underwriters by Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C., Boston, Massachusetts.

EXPERTS

The consolidated financial statements of EXACT Sciences Corporation at December 31, 2002, and for the year then ended, incorporated by reference in this prospectus supplement and accompanying prospectus have been audited by Ernst & Young LLP, independent auditors, and at December 31, 2001 and for each of the two years in the period ended December 31, 2001, by Arthur Andersen LLP, independent auditors, as set forth in their respective reports thereon included therein, and incorporated herein by reference. Such consolidated financial statements are incorporated herein by reference in reliance upon such reports given on the authority of such firms as experts in accounting and auditing.

We have been unable to obtain, after reasonable efforts, the written consent of Arthur Andersen LLP to our naming it as an expert and as having audited the consolidated financial statements for the year ended December 31, 2001 and including its audit report in this prospectus supplement and accompanying prospectus. Under these circumstances, Rule 437(a) under the Securities Act permits this registration statement to be filed without the consent of Arthur Andersen LLP. This lack of consent may limit your ability to recover damages from Arthur Andersen LLP under Section 11 of the Securities Act for any untrue statements of material fact contained in the financial statements audited by Arthur Andersen LLP or any omissions to state a material fact required to be stated therein or necessary to make the statements therein not misleading.

WHERE YOU CAN FIND MORE INFORMATION

The SEC allows us to incorporate by reference information into this prospectus supplement and the accompanying prospectus. This allows us to disclose important information to you by referring you to another document filed separately with the SEC. The information that we incorporated by reference is considered to be part of this prospectus supplement and the accompanying prospectus, and later information that we file with the SEC will automatically update and supersede the information in this prospectus supplement and the accompanying prospectus. In addition to those documents incorporated by reference in the accompanying prospectus, we incorporate by reference the following documents which have been filed with the SEC:

our Annual Report on Form 10-K for the fiscal year ended December 31, 2002, including those portions incorporated by reference therein from our definitive proxy materials on Schedule 14A as filed with the SEC on April 28, 2003;

our Quarterly Reports on Form 10-Q for the fiscal quarters ended March 31, 2003, June 30, 2003 and September 20, 2003;

the description of our common stock contained in Item 1 of our Registration Statement on Form 8-A filed with the SEC on December 26, 2000, including any amendments or reports filed for the purpose of updating the description; and

our Current Reports on Form 8-K filed with the SEC on April 24, 2003 and October 22, 2003.

We also are incorporating by reference any future filings made by us with the SEC under Section 13(a), 13(c), 14 or 15(d) of the Exchange Act, as amended, until the termination of the offering by this prospectus supplement and the accompanying prospectus. Current Reports on Form 8-K

containing only Regulation FD or Regulation G disclosure furnished under Item 9 or 12 of Form 8-K are not incorporated herein by reference.

You can obtain a copy of any documents which are incorporated by reference in this prospectus supplement and the accompanying prospectus (other than an exhibit to a filing unless that exhibit is specifically incorporated by reference into that filing) at no cost, by writing or telephoning Investor Relations, at EXACT Sciences Corporation, 100 Campus Drive, Marlborough, Massachusetts 01752, (508) 683-1200, or through our web site, at the investor relations tab, at www.exactsciences.com.

EXACT SCIENCES CORPORATION

$100,000,000

Common Stock
Preferred Stock
Subordinated Debt Securities
Senior Debt Securities
Warrants

This prospectus relates to common stock, preferred stock, subordinated debt securities, senior debt securities and warrants that we may sell from time to time in one or more offerings up to an aggregate public offering amount of $100,000,000 (or its equivalent in foreign or composite currencies) on terms to be determined at the time of sale. We will provide specific terms of the securities in supplements to this prospectus. You should read this prospectus and any supplement carefully before you invest. This prospectus may not be used to offer and sell securities unless accompanied by a prospectus supplement for the securities.

Our common stock is traded on the Nasdaq National Market under the symbol "EXAS." Each prospectus supplement to this prospectus will contain information, where applicable, as to any other listing on any national securities exchange or The Nasdaq Stock Market of the securities covered by such prospectus supplement.

These securities may be sold directly by us, through dealers or agents designated from time to time, to or through underwriters or through a combination of these methods. See "Plan of Distribution" in this prospectus. We may also describe the plan of distribution for any particular offering of these securities in any applicable prospectus supplement. If any agents, underwriters or dealers are involved in the sale of any securities in respect of which this prospectus is being delivered, we will disclose their names and the nature of our arrangements with them in a prospectus supplement. The net proceeds that we expect to receive from any such sale will also be included in a prospectus supplement.

Investing in our securities involves a high degree of risk. See "Risk Factors" on page 1 of this prospectus. We may also include risk factors in an applicable prospectus supplement under the heading "Risk Factors." You should review that section of the prospectus supplement for a discussion of matters that investors in our securities should consider.

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

The date of this prospectus is September 25, 2003.

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YOU SHOULD RELY ONLY ON THE INFORMATION CONTAINED IN THIS PROSPECTUS, ANY PROSPECTUS SUPPLEMENT OR ANY DOCUMENT INCORPORATED HEREIN OR THEREIN TO WHICH WE HAVE REFERRED YOU. WE HAVE NOT AUTHORIZED ANYONE ELSE TO PROVIDE YOU WITH INFORMATION THAT IS DIFFERENT. THIS PROSPECTUS AND ANY PROSPECTUS SUPPLEMENT MAY BE USED ONLY WHERE IT IS LEGAL TO SELL THESE SECURITIES. THE INFORMATION IN THIS PROSPECTUS OR ANY PROSPECTUS SUPPLEMENT IS CURRENT ONLY AS OF THE DATE ON THE FRONT OF THESE DOCUMENTS.

ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission, or the SEC, using a "shelf" registration process. Under this shelf process, we may sell any combination of the securities described in this prospectus in one or more offerings up to a total public offering price of $100,000,000 (or its equivalent in foreign or composite currencies). This prospectus provides you with a general description of the securities we may offer.

Each time we sell securities, we will provide a prospectus supplement that will contain specific information about the securities being offered and the terms of that offering. The prospectus supplement may also add to, update or change information contained in this prospectus. You should read both this prospectus and any prospectus supplement together with the additional information described under the heading "Where You Can Find More Information" carefully before making an investment decision.

Unless the context otherwise requires, in this prospectus, "EXACT Sciences," "the Company," "we," "us" and "our" refer to EXACT Sciences Corporation and its subsidiaries.

ABOUT EXACT SCIENCES CORPORATION

EXACT Sciences Corporation has developed and continues to develop proprietary technologies in applied genomics (our "PreGen technologies") that we believe will revolutionize the early detection of colorectal cancer and potentially other types of common cancers. We believe that medical practitioners will order tests based on our PreGen technologies as part of a regular screening program for the early detection of these cancers. We also believe that the widespread and regular application of tests utilizing our PreGen technologies will reduce mortality, morbidity and the costs associated with these cancers.

We have selected colorectal cancer as the first application of our PreGen technologies because it is the most deadly cancer among non-smokers, it is curable if detected early and it is well understood from a genomics point of view. There are over 80 million Americans age 50 and over for whom the American Cancer Society recommends regular colorectal cancer screening. Current detection methods for colorectal cancer have proven to be inadequate as screening tools due to invasiveness, inadequate performance characteristics, or poor patient compliance.

We were incorporated in the State of Delaware on February 10, 1995 as Lapidus Medical Systems, Inc. We changed our corporate name to EXACT Laboratories, Inc. on December 11, 1996, to EXACT Corporation on September 12, 2000 and to EXACT Sciences Corporation on December 1, 2000. Our principal executive offices are located at 100 Campus Drive, Marlborough, Massachusetts 01752 and our telephone number is (508) 683-1200. Our Internet address is *www.exactsciences.com.* We make available on our Internet website free of charge a link to our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and amendments to those reports as soon as practicable after we electronically file such material with the SEC. The information contained on our website is not incorporated by reference in this prospectus.

RISK FACTORS

The prospectus supplement applicable to each type or series of securities we offer will contain a discussion of the risks applicable to an investment in EXACT Sciences and to the particular types of securities that we are offering under that prospectus supplement. Prior to making a decision about investing in our securities, you should carefully consider the specific factors discussed under the caption "Risk Factors" in the applicable prospectus supplement, together with all of the other information contained or incorporated by reference in the prospectus supplement or appearing or incorporated by reference in this prospectus. You should also consider the risks, uncertainties and assumptions discussed under the caption "Management's Discussion and Analysis of Financial Condition and Results of Operations Certain Business Risks" included in our Annual Report on Form 10-K for our latest fiscal year, and our subsequent Form 10-Q's, which are incorporated by reference in this prospectus, and which may be amended, supplemented or superseded from time to time by other reports we file with the SEC in the future.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and any accompanying prospectus supplement (including any document incorporated by reference herein or therein) include forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, or the Exchange Act, that are subject to the "safe harbor" created by those sections. Some of the forward-looking statements can be identified by the use of forward-looking terms such as "believes," "expects," "may," "will," "should," "could," "seek," "intends," "plans," "estimates," "anticipates" or other comparable terms. Forward-looking statements involve inherent risks and uncertainties, which are difficult to predict and many of which are beyond our control. A number of important factors could cause actual results to differ materially from those in the forward-looking statements, including those factors discussed in "Risk Factors" in any prospectus supplement and in the documents incorporated by reference herein or therein. Factors that could cause actual results to differ from those reflected in forward-looking statements relating to our operations and business include:

- the failure to meet expectations with respect to our future performance;
- our dependence on collaborative relationships;
- our ability to license certain technologies or maintain our license agreements;
- our dependence on third parties for the supply of raw materials;
- pricing pressures and other competitive factors;
- demand for and market acceptance of our products and services;
- successful development of products and services and the timing of product and service introductions;
- reliance on third party payors to provide adequate reimbursements;
- the availability and extent of utilization of manufacturing capacity and raw materials;
- failure to comply with U.S. Food and Drug Administration requirements;

our ability to develop and implement new technologies;

our ability to protect our intellectual property;

changes in healthcare policy;

our ability to attract and retain qualified personnel;

our reliance on financial markets for future capital requirements;

the impact of new accounting policies;

the uncertainties of litigation; and

other risks and uncertainties, including those set forth or incorporated in this prospectus or any prospectus supplement, and those detailed from time to time in our filings with the Securities and Exchange Commission.

You should read this prospectus and any accompanying prospectus supplement and the documents incorporated by reference herein and therein completely and with the understanding that actual future results may be materially different from expectations. All forward-looking statements made or incorporated by reference in this prospectus and in any accompanying prospectus supplement are qualified by these cautionary statements. These forward-looking statements are made only as of the date of this prospectus, or the related prospectus supplement, as applicable, and we do not undertake any obligation, other than as may be required by law, to update or revise any forward-looking statements to reflect changes in assumptions, the occurrence of unanticipated events or changes in future operating results over time.

USE OF PROCEEDS

Unless we tell you otherwise in a prospectus supplement, we will use the net proceeds from the sale of these securities for research and development and product marketing, and other general corporate purposes, which may also include acquisitions, investments, capital expenditures, repurchase of our capital stock, and for any other purposes that we may specify in any prospectus supplement. We may also invest the net proceeds temporarily in short-term securities until we use them for their stated purpose.

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

The following table sets forth our ratio of earnings to fixed charges and earnings to combined fixed charges and preferred stock dividends for each of the periods indicated:

	SIX MONTHS ENDED JUNE 30, 2003	FISCAL YEAR ENDED DECEMBER 31,				
		2002	2001	2000	1999	1998
RATIO OF EARNINGS TO FIXED CHARGES	(1)	(1)	(1)	(1)	(1)	(1)
RATIO OF EARNINGS TO COMBINED FIXED CHARGES AND	(2)	(2)	(2)	(3)	(3)	(3)

	SIX MONTHS ENDED JUNE 30, 2003	FISCAL YEAR ENDED DECEMBER 31,
PREFERRED STOCK DIVIDENDS		

(1) During each of these periods, our earnings were less than our fixed charges. The amount of such deficiency was approximately $15.8 million for the six months ended June 30, 2003, and $29.9 million, $23.5 million, $11.9 million, $5.0 million and $3.6 million for fiscal years 2002, 2001, 2000, 1999 and 1998, respectively.

(2) During each of these periods, the Company had no preferred stock outstanding.

(3) During each of these periods, our earnings were less than our combined fixed charges and preferred dividends. The amount of such deficiency was approximately $11.9 million, $5.0 million and $3.6 million for fiscal years 2000, 1999 and 1998, respectively, or the same amounts reflected in Ratio of Earnings to Fixed Charges above, as dividends were at the discretion of the board of directors none of which were declared.

DESCRIPTION OF COMMON STOCK AND PREFERRED STOCK

The following description of our common stock and preferred stock, together with the additional information included in any applicable prospectus supplements, summarizes the material terms and provisions of these types of securities but is not complete. For the complete terms of our common stock and preferred stock, please refer to our Sixth Amended and Restated Certificate of Incorporation and our Amended and Restated By-laws, that are incorporated by reference into the registration statement which includes this prospectus and, with respect to preferred stock, the certificate of designation which will be filed with the SEC for each series of preferred stock we may designate, if any.

We will describe in a prospectus supplement the specific terms of any common stock or preferred stock that we may offer pursuant to this prospectus. If indicated in a prospectus supplement, the terms of such common stock or preferred stock may differ from the terms described below.

We have 105,000,000 shares of capital stock authorized under our certificate of incorporation, consisting of 100,000,000 shares of common stock and 5,000,000 shares of preferred stock. As of September 5, 2003, we had 19,218,608 shares of common stock outstanding and no shares of preferred stock outstanding. The authorized shares of common stock and preferred stock are available for issuance without further action by our stockholders, unless such action is required by applicable law or the rules of any stock exchange or automated quotation system on which our securities may be listed or traded. If the approval of our stockholders is not so required, our board of directors may determine not to seek stockholder approval.

Common Stock

Holders of our common stock are entitled to such dividends as may be declared by our board of directors out of funds legally available for such purpose, subject to any preferential dividend rights of any then outstanding preferred stock. The shares of common stock are neither redeemable or convertible. Holders of common stock have no preemptive or subscription rights to purchase any securities of EXACT Sciences.

In the event of our liquidation, dissolution or winding up, the holders of our common stock are entitled to receive pro rata the assets of EXACT Sciences which are legally available for distribution, after payments of all debts and other liabilities and subject to the prior rights of any holders of preferred stock then outstanding.

Each holder of our common stock is entitled to one vote for each such share outstanding in the holder's name. No holder of common stock is entitled to cumulate votes in voting for directors.

Our common stock is listed on the Nasdaq National Market under the symbol "EXAS." American Stock Transfer & Trust Company is the transfer agent and registrar for our common stock. Its address is 59 Maiden Lane, New York, NY 10038, and its telephone number is

(800) 937-5449.

Preferred Stock

Our certificate of incorporation permits us to issue up to 5,000,000 shares of preferred stock in one or more series and with rights and preferences that may be fixed or designated by our board of directors without any further action by our stockholders. The designation, powers, preferences, rights and qualifications, limitations and restrictions of the preferred stock of each series will be fixed by the certificate of designation relating to such series, which will specify the terms of the preferred stock, including:

the designation of the series, which may be by distinguishing number, letter or title;

the number of shares of the series, which number the board of directors may thereafter (except where otherwise provided in the preferred stock designation) increase or decrease (but not below the number of shares thereof then outstanding);

whether dividends, if any, shall be cumulative or noncumulative and the dividend rate of the series;

the dates on which dividends, if any, shall be payable;

the redemption rights and price or prices, if any, for shares of the series;

the terms and amount of any sinking fund provided for the purchase or redemption of shares of the series;

the amounts payable on shares of the series in the event of any voluntary or involuntary liquidation, dissolution or winding up of the affairs of EXACT Sciences;

whether the shares of the series shall be convertible into shares of any other class or series, or any other security, of EXACT Sciences or any other corporation, and, if so, the specification of such other class or series or such other security, the conversion price or prices or rate or rates, any adjustments thereof, the date or dates as of which such shares shall be convertible and all other terms and conditions upon which such conversion may be made;

restrictions on the issuance of shares of the same series or of any other class or series; and

the voting rights, if any, of the holders of shares of the series, provided that no share of preferred stock of any series will be entitled to more than one vote per share of preferred stock.

Although our board of directors has no intention at the present time of doing so, it could issue a series of preferred stock that could, depending on the terms of such series, impede the completion of a merger, tender offer or other takeover attempt.

Certain Provisions in our Certificate of Incorporation and By-laws

The following is a summary of certain provisions of Delaware law, our certificate of incorporation and our by-laws. This summary does not purport to be complete and is qualified in its entirety by reference to the corporate law of Delaware and our certificate of incorporation and by-laws.

Our certificate of incorporation and by-laws contain various provisions intended to promote the stability of our stockholder base and render more difficult certain unsolicited or hostile attempts to take us over that could disrupt EXACT Sciences, divert the attention of our directors, officers and employees and adversely affect the independence and integrity of our business.

Pursuant to our certificate of incorporation, the number of directors is fixed by our board of directors. Our directors are divided into three classes, each class to serve a three year term and to consist as nearly as possible of one third of the directors. Pursuant to our by-laws, directors elected by stockholders at an annual meeting of stockholders will be elected by a plurality of all votes cast.

Our by-laws provide that a special meeting of stockholders may be called only by the chairman of the board, a majority of the entire board of directors or the president. Stockholders are not permitted to call, or to require that the board of directors call, a special meeting of stockholders. Moreover, the business permitted to be conducted at any special meeting of stockholders is limited to the business brought before the meeting pursuant to the notice of the meeting given. In addition, our certificate of incorporation provides that any action taken by our stockholders must be effected at an annual or special meeting of stockholders and may not be taken by written consent instead of a meeting. Our by-laws establish an advance notice procedure for stockholders to nominate candidates for election as directors or to bring other business before meetings of our stockholders.

Our certificate of incorporation requires the affirmative vote of the holders of at least 80% of the voting power of all the then outstanding shares of our capital stock entitled to vote generally in the election of directors, voting together as a single class, to amend or repeal any provision of our by-laws, amend or repeal the provision of our certificate of incorporation relating to amendments to our by-laws or adopt any provision inconsistent with such provisions.

Our certificate of incorporation requires the affirmative vote of the holders of at least 75% of the voting power of all of the then outstanding shares of our capital stock entitled to vote generally in the election of directors, voting together as a single class, to amend or repeal, the provisions of our certificate of incorporation relating to the election of directors, the classified board, or the right to act by written consent or to adopt any provision inconsistent with such provisions.

We are also subject to a Delaware statute regulating "business combinations," defined to include a broad range of transactions, between Delaware corporations and "interested stockholders," defined as persons who have acquired at least 15% of a corporation's stock. Under such statute, a corporation may not engage in any business combination with any interested stockholder for a period of three years after the date such person became an interested stockholder unless certain conditions are satisfied. The statute contains provisions enabling a corporation to avoid the statute's restrictions. We have not sought to "elect out" of the statute. Therefore, the restrictions imposed by such statute will apply to us.

DESCRIPTION OF DEBT SECURITIES

General

The debt securities that we may issue will constitute debentures, notes, bonds or other evidences of indebtedness of EXACT Sciences, to be issued in one or more series, which may include senior debt securities, subordinated debt securities and senior subordinated debt securities. The particular terms of any series of debt securities we offer, including the extent to which the general terms set forth below may be applicable to a particular series, will be described in a prospectus supplement relating to such series.

Debt securities that we may issue will be issued under an indenture between us and U.S. Bank National Association, as trustee. This prospectus refers to U.S. Bank National Association as the trustee. We have filed the form of the indenture as an exhibit to the registration statement of which this prospectus is a part. If we enter into any indenture supplement, we will file a copy of that supplement with the SEC.

THE FOLLOWING DESCRIPTION IS A SUMMARY OF THE MATERIAL PROVISIONS OF THE INDENTURE. IT DOES NOT RESTATE THE INDENTURE IN ITS ENTIRETY. THE INDENTURE IS GOVERNED BY THE TRUST INDENTURE ACT OF 1939, AS AMENDED. THE TERMS OF THE DEBT SECURITIES INCLUDE THOSE STATED IN THE INDENTURE AND THOSE MADE PART OF THE INDENTURE BY REFERENCE TO THE TRUST INDENTURE ACT. WE URGE YOU TO READ THE INDENTURE BECAUSE IT, AND NOT THIS DESCRIPTION, DEFINES YOUR RIGHTS AS A HOLDER OF THE DEBT SECURITIES.

The indenture contains no covenant or provision which affords debt holders protection in the event of a highly leveraged transaction.

Information You Will Find In The Prospectus Supplement

The indenture provides that we may issue debt securities from time to time in one or more series by resolution of our board of directors or by means of a supplemental indenture, and that we may denominate the debt securities and make them payable in foreign currencies. The indenture does not limit the aggregate principal amount of debt securities that can be issued thereunder. The prospectus supplement for a series of debt securities will provide information relating to the terms of the series of debt securities being offered, which may include:

the title and denominations of the debt securities of the series;

the currency or currencies in which payment of the principal and premium, if any, and interest with respect to debt securities of the series will be payable, or in which the debt securities of the series shall be denominated, and the particular provisions applicable thereto in accordance with the indenture;

any limit on the aggregate principal amount of the debt securities of the series;

the date or dates on which the principal and premium, if any, with respect to the debt securities of the series are payable or the method of determination thereof;

the rate or rates, which may be fixed or variable, at which the debt securities of the series shall bear interest, if any, or the method of calculating and/or resetting such rate or rates of interest;

the dates from which such interest shall accrue or the method by which such dates shall be determined and the duration of the extensions and the basis upon which interest shall be calculated;

the interest payment dates for the series of debt securities or the method by which such dates will be determined, the terms of any deferral of interest and any right of ours to extend the interest payments periods;

the place or places where the principal and interest on the series of debt securities will be payable;

the terms and conditions upon which debt securities of the series may be redeemed, in whole or in part, at our option or otherwise;

our obligation, if any, to redeem, purchase, or repay debt securities of the series pursuant to any sinking fund or other specified event or at the option of the holders and the terms of any such redemption, purchase, or repayment;

the terms, if any, upon which the debt securities of the series may be convertible into or exchanged for other securities, including, among other things, the initial conversion or exchange price or rate and the conversion or exchange period;

if the amount of principal, premium, if any, or interest with respect to the debt securities of the series may be determined with reference to an index or formula, the manner in which such amounts will be determined;

if any payments on the debt securities of the series are to be made in a currency or currencies (or by reference to an index or formula) other than that in which such securities are denominated or designated to be payable, the currency or currencies (or index or formula) in which such payments are to be made and the terms and conditions of such payments;

any changes or additions to the provisions of the indenture dealing with defeasance, including any additional covenants that may be subject to our covenant defeasance option;

the portion of the principal amount of debt securities of the series which will be payable upon declaration of acceleration or provable in bankruptcy or the method by which such portion or amount shall be determined;

whether the debt securities of the series will be secured or guaranteed and, if so, on what terms;

any addition to or change in the events of default with respect to the debt securities of the series;

the identity of any trustees, authenticating or paying agents, transfer agents or registrars;

the applicability of, and any addition to or change in, the covenants currently set forth in the indenture;

the subordination, if any, of the debt securities of the series and terms of the subordination;

any other terms of the debt securities of the series which are not prohibited by the indenture; and

whether securities of the series shall be issuable as registered securities or bearer securities (with or without interest coupons), and any restrictions applicable to the offering, sale or delivery of any such bearer securities and the terms upon which such bearer securities of a series may be exchanged for registered securities, and vice versa.

Holders of debt securities may present debt securities for exchange in the manner, at the places, and subject to the restrictions set forth in the debt securities, the indenture, and the prospectus supplement. We will provide these services without charge, other than any tax or other governmental charge payable in connection therewith, but subject to the limitations provided in the indenture, any

board resolution establishing such debt securities and any applicable indenture supplement. Debt securities in bearer form and the coupons, if any, appertaining thereto will be transferable by delivery.

Senior Debt

We may issue senior debt securities under the indenture and any coupons that will constitute part of our senior debt. Unless otherwise set forth in the applicable indenture supplement or board resolution establishing such debt securities and described in a prospectus supplement, the senior debt securities will be senior unsecured obligations, ranking equally with all of our existing and future senior unsecured debt. The senior debt securities will be senior to all of our subordinated debt and junior to any secured debt we may incur as to the assets securing such debt.

Subordinated Debt

We may issue subordinated debt securities under the indenture and any coupons that will constitute part of such subordinated debt. These subordinated debt securities will be subordinate and junior in right of payment, to the extent and in the manner set forth in the indenture and any applicable indenture supplement, to all of our senior indebtedness.

If this prospectus is being delivered in connection with a series of subordinated debt securities, the accompanying prospectus supplement or the information incorporated by reference will set forth the approximate amount of senior indebtedness outstanding as of the end of the most recent fiscal quarter.

Senior Subordinated Debt

We may issue senior subordinated debt securities under the indenture and any coupons that will constitute part of our senior subordinated debt. These senior subordinated debt securities will be, to the extent and in the manner set forth in the indenture, subordinate and junior in right of payment to all of our "senior indebtedness" and senior to our other subordinated debt. See the discussions above under " Senior Debt" and " Subordinated Debt" for a more detailed explanation of our senior and subordinated indebtedness.

Interest Rate

Debt securities that bear interest will do so at a fixed rate or a floating rate. We may sell, at a discount below the stated principal amount, any debt securities which bear no interest or which bear interest at a rate that at the time of issuance is below the prevailing market rate. The relevant prospectus supplement will describe the special United States federal income tax considerations applicable to:

any discounted debt securities; and

any debt securities issued at par which are treated as having been issued at a discount for United States federal income tax purposes.

Registered Global Securities

We may issue registered debt securities of a series in the form of one or more fully registered global securities. We will deposit the registered global security with a depositary or with a nominee for a depositary identified in the prospectus supplement relating to such series. The global security or global securities will represent and will be in a denomination or aggregate denominations equal to the portion of the aggregate principal amount of outstanding registered debt securities of the series to be represented by the registered global security or securities. Unless 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 in three cases:

by the depositary for the registered global security to a nominee of the depositary;

by a nominee of the depositary to the depositary or another nominee of the depositary; and

by the depositary or any nominee to a successor of the depositary or a nominee of the successor.

The prospectus supplement relating to a series of debt securities will describe the specific terms of the depositary arrangement concerning any portion of that series of debt securities to be represented by a registered global security. We anticipate that the following provisions will generally apply to all depositary arrangements.

Upon the issuance of a registered global security, the depositary will credit, on its book-entry registration and transfer system, the principal amounts of the debt securities represented by the registered global security to the accounts of persons that have accounts with the depositary. These persons are referred to as "participants." Any underwriters, agents or debtors participating in the distribution of debt securities represented by the registered global security will designate the accounts to be credited. Only participants or persons that hold interests through participants will be able to beneficially own interests in a registered global security. The depositary for a global security will maintain records of beneficial ownership interests in a registered global security for participants. Participants or persons that hold through participants will maintain records of beneficial ownership interests in a global security for persons other than participants. These records will be the only means to transfer beneficial ownership in a registered global security.

The laws of some states may require that specified 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 global securities.

So long as the depositary, or its nominee, is the registered owner of a registered global security, the depositary or its nominee 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:

- may not have the debt securities represented by a registered global security registered in their names;
- will not receive or be entitled to receive physical delivery of debt securities represented by a registered global security in definitive form; and
- will not be considered the owners or holders of debt securities represented by a registered global security under the indenture.

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

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 which a holder is entitled to give or take under the indenture, the depositary for the registered global security would authorize the participants holding the relevant beneficial interests to give or take the action, and the participants would authorize beneficial owners owning through the participants to give or take the action or would otherwise act upon the instructions of beneficial owners holding through them.

Payment of Interest on and Principal of Registered Global Securities

We will make principal, premium, if any, and interest payments on debt securities represented by a registered global security registered in the name of a depositary or its nominee to the depositary or its nominee as the registered owner of the registered global security. None of EXACT Sciences, the trustee, or any paying agent for debt securities represented by a registered global security will have any responsibility or liability for:

- any aspect of the records relating to, or payments made on account of, beneficial ownership interests in such registered global security;
- maintaining, supervising, or reviewing any records relating to beneficial ownership interests;
- the payments to beneficial owners of the global security of amounts paid to the depositary or its nominee; or
- any other matter relating to the actions and practices of the depositary, its nominee or any of its participants.

We expect that the depositary, upon receipt of any payment of principal, premium or interest in respect of the global security, will immediately credit participants' accounts with payments in amounts proportionate to their beneficial interests in the principal amount of a registered global security as shown on the depositary's records. We also expect that payments by participants to owners of beneficial interests in a registered global security held through participants will be governed by standing instructions and customary practices. This is currently the case with the securities held for the accounts of customers registered in "street name." Such payments will be the responsibility of participants.

Exchange of Registered Global Securities

We may issue debt securities in definitive form in exchange for the registered global security if both of the following occur:

the depositary for any debt securities represented by a registered global security is at any time unwilling or unable to continue as depositary or ceases to be a clearing agency registered under the Exchange Act; and

we do not appoint a successor depositary within 90 days.

In addition, we may, at any time, determine not to have any of the debt securities of a series represented by one or more registered global securities. In this event, we will issue debt securities of that series in definitive form in exchange for all of the registered global security or securities representing those debt securities.

Covenants by EXACT Sciences

The indenture includes covenants by us, including among other things that we will make all payments of principal and interest at the times and places required. The board resolution or supplemental indenture establishing each series of debt securities may contain additional covenants, including covenants which could restrict our right to incur additional indebtedness or liens and to take certain actions with respect to our businesses and assets.

Events of Default

Unless otherwise indicated in the applicable prospectus supplement, the following will be events of default under the indenture with respect to each series of debt securities issued under the indenture:

(a) failure to pay when due any interest on any debt security of that series, continued for 30 days;

(b) failure to pay when due the principal of, or premium, if any, on, any debt security of that series;

(c) default in the payment of any sinking fund installment with respect to any debt security of that series when due and payable;

(d) failure to perform any other covenant or agreement of ours under the indenture or the supplemental indenture with respect to that series or the debt securities of that series, continued for 90 days after written notice to us by the trustee or holders of at least 25% in aggregate principal amount of the outstanding debt securities of the series to which the covenant or agreement relates;

(e) certain events of bankruptcy, insolvency or similar proceedings affecting us; and

(f) any other event of default specified in any supplemental indenture under which such series of debt securities is issued.

Except as to certain events of bankruptcy, insolvency or similar proceedings affecting us and except as provided in the applicable prospectus supplement, if any event of default shall occur and be continuing with respect to any series of debt securities under the indenture, either the trustee or the holders of at least 25% in aggregate principal amount of outstanding debt securities of such series may accelerate the maturity of all debt securities of such series. Upon certain events of bankruptcy, insolvency or similar proceedings affecting us, the principal, premium, if any, and interest on all debt securities of each series shall be immediately due and payable.

After any such acceleration, but before a judgment or decree based on acceleration has been obtained by the trustee, the holders of a majority in aggregate principal amount of each affected series of debt securities may waive all defaults with respect to such series and rescind and annul such acceleration if all events of default, other than the non-payment of accelerated principal, have been cured, waived or otherwise

remedied.

No holder of any debt securities will have any right to institute any proceeding with respect to the indenture or for any remedy under the indenture, unless such holder shall have previously given to the trustee written notice of a continuing event of default and the holders of at least 25% in aggregate principal amount of the outstanding debt securities of the relevant series shall have made written request and offered indemnity satisfactory to the trustee to institute such proceeding as trustee, and the trustee shall not have received from the holders of a majority in aggregate principal amount of the outstanding debt securities of such series a direction inconsistent with such request and shall have failed to institute such proceeding within 60 days. However, such limitations do not apply to a suit instituted by a holder of a debt security for enforcement of payment of the principal of and premium, if any, or interest on such debt security on or after the respective due dates expressed in such debt security.

Supplemental Indentures

We and the trustee may, at any time and from time to time, without prior notice to or consent of any holders of debt securities, enter into one or more supplemental indentures to, among other things:

add guarantees to or secure any series of debt securities;

provide for the succession of another person pursuant to the provisions of the indenture relating to consolidations, mergers and sales of assets and the assumption by such successor of our covenants, agreements, and obligations, or to otherwise comply with the provisions of the indenture relating to consolidations, mergers, and sales of assets;

surrender any right or power conferred upon us under the indenture or to add to our covenants further covenants, restrictions, conditions or provisions for the protection of the holders of all or any series of debt securities;

cure any ambiguity or to correct or supplement any provision contained in the indenture, in any supplemental indenture or in any debt securities that may be defective or inconsistent with any other provision contained therein;

modify or amend the indenture in such a manner as to permit the qualification of the indenture or any supplemental indenture under the Trust Indenture Act;

add to or change any of the provisions of the indenture to permit the defeasance and discharge of any series of debt securities pursuant to the indenture, so long as any such action does not adversely affect the interests of the holders of debt securities of any series in any material respect;

add to, change, or eliminate any of the provisions of the indenture with respect to one or more series of debt securities, so long as any such addition, change or elimination shall not apply to any debt securities of any series created prior to the execution of such supplemental indenture and entitled to the benefit of such provision;

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

establish the form or terms of debt securities of any series and to make any change that does not adversely affect the interests of the holders of debt securities.

With the consent of the holders of at least a majority in principal amount of debt securities of each series affected by such supplemental indenture (each series voting as one class), we and the trustee may enter into one or more supplemental indentures for the purpose of adding any provisions to or changing in any manner or eliminating any of the provisions of the indenture or modifying in any manner the rights of the holders of debt securities of each such series.

Notwithstanding our rights and the rights of the trustee to enter into one or more supplemental indentures with the consent of the holders of debt securities of the affected series as described above, no such supplemental indenture shall, without the consent of the holder of each outstanding debt security of the affected series, among other things:

change the final maturity of the principal of, or any installment of interest on, any debt securities;

reduce the principal amount of any debt securities or the rate of interest on any debt securities;

change the currency in which any debt securities are payable;

release any security interest that may have been granted with respect to such debt securities;

impair the right of the holders to conduct a proceeding for any remedy available to the trustee;

reduce the percentage in principal amount of any series of debt securities whose holders must consent to an amendment or supplemental indenture;

modify the ranking or priority of the securities;

reduce any premium payable upon the redemption of any debt securities or change the time at which any debt security may be redeemed; or

make any change that adversely affects the relative rights of holders of subordinated debt securities with respect to senior debt securities.

Satisfaction and Discharge of the Indenture; Defeasance

Except to the extent set forth in a supplemental indenture with respect to any series of debt securities, we, at our election, may discharge the indenture and the indenture shall generally cease to be of any further effect with respect to that series of debt securities if (a) we have delivered to the trustee for cancellation all debt securities of that series (with certain limited exceptions) or (b) all debt securities of that series not previously delivered to the trustee for cancellation shall have become due and payable, or are by their terms to become due and payable within one year or are to be called for redemption within one year, and we have deposited with the trustee the entire amount sufficient to pay at maturity or upon redemption all such debt securities.

In addition, we have a "legal defeasance option" (pursuant to which we may terminate, with respect to the debt securities of a particular series, all of our obligations under such debt securities and the indenture with respect to such debt securities) and a "covenant defeasance option" (pursuant to which we may terminate, with respect to the debt securities of a particular series, our obligations with respect to such debt securities under certain specified covenants contained in the indenture). If we exercise our legal defeasance option with respect to a series of debt securities, payment of such debt securities may not be accelerated because of an event of default. If we exercise our covenant defeasance option with respect to a series of debt securities, payment of such debt securities may not be accelerated because of an event of default related to the specified covenants.

We may exercise our legal defeasance option or our covenant defeasance option with respect to the debt securities of a series only if we irrevocably deposit in trust with the trustee cash or U.S. government obligations (as defined in the indenture) for the payment of principal, premium, if any, and interest with respect to such debt securities to maturity or redemption, as the case may be. In addition, to exercise either of our defeasance options, we must comply with certain other conditions, including the delivery to the trustee of an opinion of counsel to the effect that the holders of debt securities of such series will not recognize income, gain or loss for Federal income tax purposes as a result of such defeasance and will be subject to Federal income tax on the same amounts, in the same manner and at the same times as would have been the

case if such defeasance had not occurred (and, in the case of legal defeasance only, such opinion of counsel must be based on a ruling from the Internal Revenue Service or other change in applicable Federal income tax law).

The trustee will hold in trust the cash or U.S. government obligations deposited with it as described above and will apply the deposited cash and the proceeds from deposited U.S. government obligations to the payment of principal, premium, if any, and interest with respect to the debt securities of the defeased series.

Mergers, Consolidations and Certain Sales of Assets

We may not

- consolidate with or merge into any other person or entity or permit any other person or entity to consolidate with or merge into us in a transaction in which we are not the surviving entity, or
- transfer, lease or dispose of all or substantially all of our assets to any other person or entity

unless:

- the resulting, surviving or transferee entity shall be a corporation organized and existing under the laws of the United States or any state thereof and such resulting, surviving or transferee entity shall expressly assume, by supplemental indenture, all of our obligations under the debt securities and the indenture;
- immediately after giving effect to such transaction (and treating any indebtedness which becomes an obligation of the resulting, surviving or transferee entity as a result of such transaction as having been incurred by such entity at the time of such transaction), no default or event of default would occur or be continuing; and
- we shall have delivered to the trustee an officers' certificate and an opinion of counsel, each stating that such consolidation, merger or transfer and such supplemental indenture (if any) comply with the indenture.

Governing Law

The indenture and the debt securities will be governed by the laws of the State of New York.

No Personal Liability of Directors, Officers, Employee