

EXACT SCIENCES CORP
Form 424B5
April 13, 2010

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

Filed Pursuant to Rule 424(b)(5)
Registration No. 333-147511

Subject to Completion, dated April 13, 2010

Prospectus Supplement
(To Prospectus dated December 3, 2007)

3,500,000 Shares

EXACT SCIENCES CORPORATION
Common Stock

We are offering 3,500,000 shares of our common stock.

Our common stock is traded on the NASDAQ Capital Market under the symbol "EXAS." On April 12, 2010, the last sale price of our common stock as reported on the NASDAQ Capital Market was \$4.73 per share.

Investing in our common stock involves risks that are described in the "Risk Factors" section beginning on page S-4 of this prospectus supplement.

	Per Share	Total
Public offering price	\$	\$
Underwriting discount	\$	\$
Proceeds, before expenses, to us	\$	\$

The underwriter may also purchase up to an additional 525,000 shares from us at the public offering price, less the underwriting discount, within 30 days from the date of this prospectus supplement to cover over-allotments.

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

The shares will be ready for delivery on or about April , 2010.

Baird

The date of this prospectus supplement is April , 2010.

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ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement and the accompanying prospectus form part of a registration statement on Form S-3 that we filed with the Securities and Exchange Commission, or the "SEC," using a "shelf" registration process. This document contains two parts. The first part consists of this prospectus supplement, which provides you with specific information about this offering. The second part, the accompanying prospectus, provides more general information, some of which may not apply to this offering. Generally, when we refer only to the "prospectus," we are referring to both parts combined.

In this prospectus supplement, the "Company," "we," "us," and "our" and similar terms refer to Exact Sciences Corporation. References to our "common stock" refer to the common stock of Exact Sciences Corporation.

This prospectus supplement, and the information incorporated herein by reference, may add, update or change information in the accompanying prospectus. You should read both this prospectus supplement and the accompanying prospectus together with additional information described under the headings "Where You Can Find More Information" and "Incorporation of Certain Information by Reference." If there is any inconsistency between the information in this prospectus supplement and the accompanying prospectus, you should rely on the information in this prospectus supplement.

You should rely only on the information contained in or incorporated by reference to this prospectus supplement and the accompanying prospectus. Neither we nor the underwriter have authorized any other person to provide information different from that contained in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein and therein. If anyone provides you with different or inconsistent information, you should not rely on it. You should assume that the information appearing in the prospectus and this prospectus supplement is accurate as of the dates on their respective covers, regardless of time of delivery of the prospectus and this prospectus supplement or any sale of securities. Our business, financial condition, results of operations and prospects may have changed since those dates.

All references in this prospectus supplement to our consolidated financial statements include, unless the context indicates otherwise, the related notes.

The industry and market data and other statistical information contained in this prospectus supplement, the accompanying prospectus and the documents we incorporate by reference are based on management's own estimates, independent publications, government publications, reports by market research firms or other published independent sources, and, in each case, are believed by management to be reasonable estimates. Although we believe these sources are reliable, we have not independently verified the information. None of the independent industry publications used in this prospectus supplement, the accompanying prospectus or the documents we incorporate by reference were prepared on our or our affiliates' behalf and none of the sources cited by us consented to the inclusion of any data from its reports, nor have we sought their consent.

CAUTIONARY STATEMENT ABOUT FORWARD LOOKING INFORMATION

Certain information set forth in this prospectus supplement, set forth in the accompanying prospectus or incorporated by reference in this prospectus supplement, may contain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended (the "Securities Act"), and Section 21E of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), that are intended to be covered by the "safe harbor" created by those sections. Forward-looking statements, which are based on certain assumptions and describe our future plans, strategies and expectations, can generally be identified by the use of forward-looking terms such as "believe," "expect," "may," "will," "should," "would," "could," "seek," "intend," "plan," "estimate," "goal," "anticipate," "project" or other comparable terms. Forward-looking statements involve inherent risks and uncertainties which could cause actual results to differ materially from those in the forward-looking statements, as a result of various factors including those risks and uncertainties included in this prospectus supplement under the caption "Risk Factors," and those risks and uncertainties described in the documents incorporated by reference into this prospectus supplement and the accompanying prospectus. We urge you to consider those risks and uncertainties in evaluating our forward-looking statements. All subsequent written and oral forward-looking statements attributable to us or to persons acting on our behalf are expressly qualified in their entirety by the applicable cautionary statements. We further caution readers not to place undue reliance upon any such forward-looking statements, which speak only as of the date made. Except as otherwise required by the federal securities laws, we disclaim any obligation or undertaking to publicly release any updates or revisions to any forward-looking statement contained herein or in the accompanying prospectus (or elsewhere) to reflect any change in our expectations with regard thereto or any change in events, conditions or circumstances on

which any such statement is based.

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SUMMARY

The information below is only a summary of more detailed information included elsewhere in or incorporated by reference in this prospectus supplement and the accompanying prospectus. This summary may not contain all the information that is important to you or that you should consider before making a decision to invest in our common stock. Please read this entire prospectus supplement and the accompanying prospectus, including the risk factors, as well as the information incorporated by reference in this prospectus supplement and the accompanying prospectus, carefully.

Our Company

Exact Sciences Corporation is a molecular diagnostics company focused on the early detection and prevention of colorectal cancer. We have exclusive intellectual property protecting our non-invasive, molecular screening technology for the detection of colorectal cancer.

Our primary goal is to become the market leader for a patient-friendly diagnostic screening product for the early detection of colorectal pre-cancer and cancer. Our strategic roadmap to achieve this goal includes the following key components:

develop and refine our non-invasive stool-based (sDNA) colorectal pre-cancer and cancer screening test;

advance our product through U.S. Food and Drug Administration, or FDA, clinical trials;

secure insurance coverage and reimbursement for our product; and

commercialize an FDA-cleared product that detects colorectal pre-cancer and cancer.

Our current focus is on the commercial development and seeking FDA clearance of our sDNA colorectal cancer screening product. We believe obtaining FDA clearance is critical to building broad demand and successful commercialization for our sDNA colorectal cancer screening technologies. As part of our product development efforts, we are exploring the marker combinations and platform requirements necessary for optimal performance of our technology based on market need. Objectives around performance, throughput and cost are among the elements that will need to be met in the design and development of a commercial product based on our technology.

Corporate Information

Our executive offices are located at 441 Charmany Drive, Madison, Wisconsin 53719. Our telephone number is 608-284-5700. Our Internet website address is <http://www.exactsciences.com>. Our Internet website and the information contained therein or connected thereto are not part of this prospectus supplement or the accompanying prospectus.

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The Offering

The summary below describes some of the terms of the offering. For a more complete description of our common stock, see "Description of Capital Stock" in the accompanying prospectus.

Issuer:	Exact Sciences Corporation
Shares of common stock offered by us:	3,500,000 shares.
Shares of common stock outstanding after the offering ⁽¹⁾ :	39,332,021 shares.
Over-allotment option:	525,000 shares.
Use of Proceeds:	We intend to use the net proceeds from this offering for general corporate and working capital purposes, including to fund strategic initiatives that we may undertake from time to time, for product development and in furtherance of our efforts to obtain FDA clearance of our sDNA colorectal cancer screening product. See "Use of Proceeds."
Dividends:	We have never paid any cash dividends on our capital stock and do not plan to pay any cash dividends in the foreseeable future.
NASDAQ Capital Market symbol:	"EXAS"
Risk Factors:	Investing in our common stock involves substantial risks. You should carefully consider all the information included or incorporated by reference in this prospectus supplement prior to investing in our common stock. In particular, we urge you to carefully consider the factors set forth under "Risk Factors."

(1) The number of shares outstanding after the offering is based on 35,832,021 shares outstanding as of March 31, 2010, and includes 115,000 shares of unvested restricted stock issued to employees, directors and consultants. The number of outstanding shares after the offering does not include, in each case as of March 31, 2010:

5,887,814 shares subject to outstanding stock options at a weighted average exercise price of \$1.77 per share;

3,133,971 additional shares of common stock reserved for issuance under our equity incentive plans; or

1,050,000 shares reserved for issuance upon the exercise of outstanding stock purchase warrants at an exercise price of \$1.90 per share.

If the underwriter's over-allotment option is exercised in full, we will issue and sell an additional 525,000 shares of our common stock and will have 39,857,021 shares outstanding after the offering.

Except as otherwise noted, all information in this prospectus supplement assumes no exercise of the underwriter's over-allotment option.

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RISK FACTORS

You should carefully consider the risks described below before making an investment decision. We cannot be certain that we will successfully address these risks. If we are unable to address these risks, our business may not grow, our stock price may suffer and/or we may be unable to stay in business. In such case, the trading price of our common stock could decline and you may lose all or part of your investment. Additional risks and uncertainties not presently known to us, which we currently deem immaterial or which are similar to those faced by other companies in our industry or business in general, may also impair our business operations. These risks and uncertainties include, but are not limited to, the following:

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

We have incurred losses since we were formed and have had only modest product and royalty fee revenues since the commercial launch of PreGen-Plus in August 2003. From our date of inception on February 10, 1995 through December 31, 2009, we have accumulated a total deficit of approximately \$181.6 million. We expect that our losses will continue for at least the next several years and we will be required to invest significant additional funds toward development of our colorectal cancer screening technology. If our revenue does not grow significantly, we will not be profitable. We cannot be certain that the revenue from the sale of any of our technologies will be sufficient to make us profitable.

Our future revenues will depend on our ability to successfully commercialize an FDA-cleared product for stool-based DNA colorectal cancer screening. Our ability to successfully commercialize our technologies may be affected by the following factors:

the scope of and progress made in our research and development activities;

our ability to successfully execute on a clinical trial;

threats posed by competing technologies;

acceptance, endorsement and formal policy approval of stool-based DNA screening reimbursement by Medicare and other third-party payors; and

our ability to commercialize our test through primary care physician awareness and consumer education and outreach.

Many of these factors are outside our control and, accordingly, we cannot assure you that one or more of the foregoing will occur in the near term, or at all. Failure to achieve one or more of the foregoing events could negatively impact the successful commercialization of stool-based DNA testing services or products utilizing our intellectual property and impair our ability to generate revenues and achieve profitability.

We will need additional capital to execute our business plan, and we may be unable to raise additional capital on acceptable terms.

Following the closing of our strategic transaction with Genzyme in January 2009, we have resumed our efforts to develop an FDA-cleared in vitro diagnostic test for stool-based DNA colorectal cancer screening. The FDA clearance path for our colorectal cancer screening technology is likely to take significant time and require significant research, development and clinical study expenditures.

Although we believe we have sufficient capital to fund our operations for at least the next twelve months, we do not have sufficient capital, even after giving effect to this offering, to fully fund the commercial development of our stool-based DNA technology and related FDA submission and commercialization efforts. We do not expect that product royalty payments or milestone payments from LabCorp will materially supplement our liquidity position in the next twelve months, if at all. If we are unable to obtain needed financing on acceptable terms, we may not be able to implement our business plan which could have a material adverse effect on our business, financial condition and results of operations. If we raise additional funds through the sale of additional equity, convertible debt or other equity-linked securities, our shareholders'

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percentage ownership in us will be further reduced. In addition, these transactions may dilute the value of our outstanding stock, including shares issued in this offering. We may issue securities that have rights, preferences and privileges senior to our common stock. If we raise additional funds through collaborations or licensing arrangements, we may relinquish rights to certain of our technologies or products, or grant licenses to third parties on terms that are unfavorable to us. Even if we successfully raise sufficient funds to continue our operations to fund the development, FDA submission, and commercialization of our technology, including an

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FDA-cleared in vitro diagnostic test for stool-based DNA colorectal cancer screening, we cannot assure you that our business will ever generate sufficient cash flow from operations to become profitable.

If Medicare and other third-party payors, including managed care organizations, do not issue positive policy decisions approving reimbursement for our stool-based DNA colorectal cancer screening technology, the commercial success of products utilizing our technologies would be compromised.

Successful commercialization of a stool-based DNA screening product will depend, in large part, on the availability of adequate reimbursement from government insurance plans, managed care organizations and private insurance plans. There is significant uncertainty concerning third-party reimbursement for the use of tests incorporating new technology. Reimbursement of stool-based DNA colorectal cancer screening 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; approved by the major guidelines organizations; reliable, safe and effective; medically necessary; appropriate for the specific patient; and cost-effective.

If we are unable to obtain positive policy decisions from third-party payors, including managed care organizations, approving reimbursement for stool-based DNA testing services or products at adequate levels, the commercial success of stool-based DNA screening for colorectal cancer would be compromised and our revenues would be significantly limited.

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 89 million Americans age 50 and above, of which we believe approximately one-half fail to strictly follow the ACS's screening guidelines for colorectal cancer. As a result, the colorectal cancer 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 procedure in which a radiologist views the inside of the colon through a scanner, as well as from existing guaic-based fecal occult blood testing, or FOBT, and improved screening tests such as immunochemical FOBT. In addition, some companies and institutions are developing serum-based tests, or screening tests based on the detection of proteins, nucleic acids or the presence of fragments of mutated genes in the blood that are produced by colon cancer. For example, it is our understanding that Epigenomics AG has completed a large multi-center study to demonstrate the performance of its blood-based screening test for colorectal cancer. Additionally, we understand OncoMethylome Sciences is in the process of enrolling patients for a large blood-based colorectal cancer screening trial. 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 tests are superior or because they may have more expertise, experience, financial resources and stronger business relationships.

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

Any future commercialization of our stool-based DNA screening technology may require that we license certain third-party intellectual property. There can be no assurance that we can obtain these licenses on acceptable terms, if at all. Furthermore, there can be no assurance that any current contractual arrangements between us and third parties or between our strategic partners and other third parties, will be continued, or not breached or terminated early, or that we will be able to enter into any future relationships necessary to the continued commercial sale of any stool-based DNA testing services or products utilizing our technologies, or necessary to our realization of material revenues. For example, we have an exclusive license from Case Western Reserve University, or Case Western, for the use of the Vimentin gene in the field of colorectal cancer testing, pursuant to which we are permitted to sublicense such rights to others. If Case Western were to terminate this agreement as a result of a breach by us or otherwise, we would lose our ability to offer any test or testing service based on the Vimentin gene, including the right to develop an FDA-cleared colorectal cancer screening product using the Vimentin gene, which would materially harm our business. Any failure to obtain necessary technologies or raw materials could require any stool-based DNA testing services or products utilizing our technologies to be re-configured which could halt such service or product entirely, negatively impact its commercial sale and increase the associated costs, any one of which could materially harm our business and adversely affect our future revenues.

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

If the results of our research and clinical studies and our sales and marketing activities relating to communication of these results, do not convince thought-leading gastroenterologists, guidelines organizations, primary care physicians, third-party payors and patients that tests using our technologies are reliable, effective and superior to existing screening methods, including Hemoccult II, Hemoccult Sensa and immunochemical FOBT, 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 prevent us from successfully commercializing our technologies.

We expect to rely on third parties to conduct any future studies of our technologies that may be required by the FDA, and those third parties may not perform satisfactorily.

We do not have the ability to independently conduct clinical or other studies that may be required to obtain clearance for our DNA-based colorectal screening technology with the FDA. Accordingly, we expect to rely on third parties such as contract research organizations, medical institutions and clinical investigators to conduct any such studies. Our reliance on these third parties for clinical development activities will reduce our control over these activities. Accordingly, these third-party contractors may not complete activities on schedule, or may not conduct studies in accordance with regulatory requirements or our study design. Our reliance on third parties that we do not control does not relieve us of our requirement to prepare, and ensure our compliance with, various procedures required under good clinical practices, even though third-party contract research organizations have prepared and are complying with their own, comparable procedures. If these third parties do not successfully carry out their contractual duties or regulatory obligations or meet expected deadlines, if the third parties need to be replaced or if the quality or accuracy of the data they obtain is compromised due to the failure to adhere to our clinical protocols or regulatory requirements or for other reasons, our studies may be extended, delayed, suspended or terminated, and we may not be able to obtain regulatory approval for our technologies.

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

Even if our technologies are superior to other colorectal cancer screening options, adequate third-party reimbursement is obtained and we convince medical practitioners to 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 ACS that all Americans age 50 and above be screened for colorectal cancer, a majority of these individuals do not complete a colorectal cancer screening test. Use of a stool-based DNA colorectal cancer screening will require people to collect a stool sample, which some people may be reluctant to do. If only a small portion of the recommended population is regularly screened for colorectal cancer or decides to utilize colorectal cancer screening tests using our technologies, we will, despite our efforts, experience limits on our revenue and our business would be materially harmed.

We may be subject to substantial costs and liability or be prevented from licensing our technologies for cancer detection 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 non-invasive early detection of colorectal cancer and is designed to maximize our patent protection against third parties in the U.S. and, potentially, in certain foreign countries. We have filed patent applications that we believe cover methods we have designed to help detect colorectal cancer and other cancers. 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 such suits or that the damages or other remedies, if any, awarded

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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 services or products containing our technologies, which would have a material adverse affect 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 U.S. 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.

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.

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. We have in the past been the subject of opposition proceedings relating to our patents. 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. Furthermore, in the life sciences field, courts frequently render opinions that may affect the patentability of certain inventions or discoveries, including opinions that may affect the patentability of isolated DNA and/or methods for analyzing or comparing DNA. Such decisions might adversely impact our ability to obtain new patents and facilitate third-party challenges to our existing patents that result in determinations that our existing patents are unenforceable or invalid.

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 or our partners fail to comply with regulatory requirements, we may be subject to stringent penalties and our business may be materially adversely affected.

The marketing and sale of stool-based DNA colorectal cancer screening services or products containing our technologies are subject to various state, federal and foreign regulations. We cannot assure you that we or our strategic partners will be able to comply with applicable regulations and regulatory guidelines. If we or our partners fail to comply with any such applicable regulations and guidelines, we could incur significant liability and/or our partners could be forced to cease offering such services or products in certain jurisdictions.

Moreover, healthcare policy has been a subject of extensive discussion in the executive and legislative branches of the federal and many state governments. Development of the existing commercialization strategy for stool-based DNA colorectal cancer screening has been based on existing healthcare policies. We cannot predict what additional 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.

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The success of our business and business strategy will be substantially dependent upon the efforts of our senior management team.

Our success will depend largely on the skills, experience and performance of key members of our senior management team. Effective April 2, 2009, Kevin T. Conroy was appointed as our new President and Chief Executive Officer. Similarly, Effective April 2, 2009, Maneesh Arora was appointed as our new Chief Financial Officer. On August 1, 2009, Dr. Graham Lidgard was hired as Chief Science Officer. Messrs. Conroy, Arora, and Dr. Lidgard are critical to directing and managing our growth and development in the future. Our success will be substantially dependent upon our senior management team's ability to gain proficiency in leading our company, implement or adapt our corporate strategies and initiatives, and develop key professional relationships, including relationships with our key collaborators and business partners. The efforts of each of these persons will be critical to us as we continue to develop our technologies and work towards the commercialization of an FDA-cleared product. If we were to lose any 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 at important research and academic institutions, such as Mayo Clinic, Case Western Reserve University, and The 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 appropriate options for colorectal cancer screening, or 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.

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 products or services based on our technologies, or activities related to our research and clinical studies, 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.

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 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.

Our stock price may be volatile.

The market price of our common stock has fluctuated widely. 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 that may affect our stock price include the various risks identified in this "Risk Factors" section.

Because we are a company with no significant operating revenue, any one of these factors may be deemed material. Sharp drops in the market price of our common stock expose us to securities class-action litigation. Such litigation could result in substantial expenses and a diversion of management's attention and resources, which would seriously harm our business, financial condition, and results of operations.

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Based on an assumed offering price of \$4.73 per share, which was the last reported sale price for our common stock on April 12, 2010, we estimate that our net proceeds from the sale of our common stock in this offering will be approximately \$15.4 million, after deducting the underwriting discount and estimated offering expenses payable by us. If the underwriter exercises its option to purchase 525,000 additional shares to cover over-allotments, we estimate that our net proceeds from the sale of our common stock in this offering will be approximately \$17.7 million, after deducting the underwriting discount and estimated offering expenses payable by us, based on an assumed offering price of \$4.73 per share.

We intend to use the net proceeds from this offering for general corporate and working capital purposes, including to fund strategic initiatives that we may undertake from time to time, for product development and in furtherance of our efforts to obtain FDA clearance of our sDNA colorectal cancer screening product.

The amounts and timing of our use of proceeds will vary depending on a number of factors, including the amount of cash generated or used by our operations, and the rate of growth, if any, of our business. As a result, we will retain broad discretion in the allocation of the net proceeds of this offering.

DILUTION

Our net tangible book value as of December 31, 2009, was \$6,094,000 or \$0.17 per share of common stock. Net tangible book value per share represents total tangible assets less total liabilities, divided by the number of shares of common stock outstanding as of December 31, 2009. After giving effect to our sale of 3,500,000 shares of common stock in this offering at an assumed offering price of \$4.73 per share, which was the last reported sale price of our common stock on April 12, 2010, and after deduction of the underwriter fees and estimated offering expenses payable by us, our net tangible book value as of December 31, 2009, would have been \$21.5 million, or \$0.55 per share. This represents an immediate increase in net tangible book value of \$0.38 per share to existing stockholders and an immediate dilution in net tangible book value of \$4.18 per share to purchasers of common stock in this offering. The following table illustrates this calculation.

Offering price per share of common stock	\$ 4.73
Net tangible book value per share as of December 31, 2009	\$ 0.17
Increase per share attributable to this offering	\$ 0.38
As adjusted tangible book value per share after this offering	\$ 0.55
Dilution per share to new investors in this offering	\$ 4.18

The number of shares of common stock outstanding used for existing stockholders in the table and calculations above is based on 35,523,140 shares outstanding as of December 31, 2009, includes 40,000 shares of unvested restricted stock issued to employees, directors and consultants, and excludes, in each case as of December 31, 2009:

5,912,019 shares subject to outstanding stock options at a weighted average exercise price of \$1.76 per share;

3,184,766 additional shares of common stock reserved for issuance under our equity incentive plans; and

1,250,000 shares reserved for issuance upon the exercise of outstanding stock purchase warrants at an exercise price of \$1.90 per share.

Table of Contents**CAPITALIZATION**

The following table sets forth our cash and cash equivalents and capitalization as of December 31, 2009, on an actual basis and on an as adjusted basis to give effect to the sale of 3,500,000 shares of common stock by us pursuant to this offering, based on an assumed offering price of \$4.73 per share, which is the last reported sale price for our common stock on April 12, 2010, and the application of the net proceeds therefrom (after deducting the underwriting discount and estimated offering expenses payable by us) as described in "Use of Proceeds." You should read this table in conjunction with the information set forth under "Use of Proceeds," included elsewhere in this prospectus supplement, and "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our consolidated financial statements and related notes to those statements, incorporated by reference into this prospectus supplement and the accompanying prospectus.

<i>(Dollars in thousands)</i>	As of December 31, 2009	
	Actual	As Adjusted
Cash and cash equivalents	\$ 21,924	\$ 37,311
Long-term debt (including current maturities)	\$ 1,000	\$ 1,000
Stockholders' equity:		
Preferred stock, \$.01 par value per share; 5,000,000 shares authorized; no shares issued and outstanding on an actual or as adjusted basis		
Common stock, \$.01 par value per share; 100,000,000 shares authorized; 35,523,140 issued and outstanding on an actual basis, and 39,023,140 shares issued and outstanding on an adjusted basis	355	390
Additional paid-in capital	187,333	202,685
Other comprehensive loss	(1)	(1)
Accumulated deficit	(181,593)	(181,593)
Total stockholders' equity	6,094	21,481
Total capitalization	\$ 7,094	\$ 22,481

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Set forth below are our executive officers and directors, together with their positions and ages as of March 31, 2010.

Name	Age	Position
Kevin T. Conroy	44	President, Chief Executive Officer and Director
Maneesh K. Arora	41	Senior Vice President and Chief Financial Officer
Graham P. Lidgard, Ph.D.	61	Senior Vice President, Chief Science Officer
Barry M. Berger, MD	58	Senior Vice President, Chief Medical Officer
James Connelly	63	Director
Sally W. Crawford	56	Director
Edwin M. Kania, Jr.	52	Director
Connie Mack, III	69	Director
Katherine Napier	55	Director
Lance Willsey, MD	48	Director
Patrick J. Zenner	63	Director

Set forth below is background information relating to our directors and executive officers.

Directors

Kevin T. Conroy has served as our President and Chief Executive Officer since April 2009 and as a director since March 2009. Mr. Conroy served as president and chief executive of Third Wave Technologies, Inc., a molecular diagnostics company, from December 2005 until the acquisition of Third Wave Technologies, Inc. by Hologic, Inc. in July 2008. He joined Third Wave Technologies in July 2004 and served as general counsel until December 2005. Prior to joining Third Wave Technologies, Mr. Conroy served as intellectual property counsel at GE Healthcare, a medical imaging and diagnostics company. Before joining GE Healthcare, Mr. Conroy was chief operating officer of two early-stage, venture-backed technology companies in Northern California. Prior to those positions, he was an intellectual property litigator at two Chicago law firms, McDermott Will & Emery, and Pattishall, McAuliffe, Newbury, Hilliard and Geraldson, where he was a partner. He earned a bachelor's of science degree in electrical engineering at Michigan State University and a J.D. from the University of Michigan.

James P. Connelly has served as a director since April 2009. Mr. Connelly has been a partner in the Foley & Lardner law firm since 1977, where he was the founding chairman of the Health Law Practice. He brings to our Board of Directors more than 25 years of experience providing strategic business and legal advice to large health care networks, clinics and laboratories. He also has advised a number of emerging biotechnology and life sciences companies. He was a director of Third Wave Technologies, Inc., a molecular diagnostics company, from 2005 until its acquisition by Hologic, Inc. in July 2008. Mr. Connelly earned his bachelor's degree from Marquette University and his law degree from the Georgetown University Law Center, where he was editor-in-chief of the Georgetown Law Journal.

Sally W. Crawford has served as a director since August 1999 and as our Chairperson from January 2006 to April 2008. Ms. Crawford was an independent healthcare consultant for Bayer HealthCare, a pharmaceutical and medical products division of Bayer AG, from 1997 to 2009. From 1979 to 1982, Ms. Crawford served as the Director of Marketing for Matthew Thornton Health Plan, and from 1982 to 1985, Ms. Crawford served as the Marketing Director for Beacon Health. From April 1985 to January 1997, Ms. Crawford served as Chief Operating Officer for Healthsource, Inc., a publicly-traded managed care organization which she co-founded. As Chief Operating Officer of Healthsource, Ms. Crawford was responsible for reviewing and establishing systems for financial reporting. Ms. Crawford also served as the Chief Executive Officer of several subsidiaries of Healthsource, including Healthsource New Hampshire, Healthsource for Seniors, Jobcare and Healthsource Administrators, and was responsible for the analysis and oversight of the subsidiaries' financial reporting. Ms. Crawford is also a director of CombinatoRx, Incorporated, Hologic, Inc., Universal American Corp. and Insulet Corporation. She was a director of Chittenden Corporation, a bank holding company, from 1998 to 2008 and of Cytoc Corporation, a medical equipment and device company, from 1998 to 2007. Ms. Crawford holds a BA in English from Smith College and an MS in communications from Boston University.

Edwin M. Kania, Jr. has served as a director since September 1995. Since 1999, Mr. Kania has been Managing Partner and Chairman of Flagship Ventures, a Boston-based venture capital firm that he co-founded and that also manages funds raised by OneLiberty Ventures. Prior to co-founding Flagship Ventures, Mr. Kania was a General Partner at OneLiberty

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Ventures. Mr. Kania was also a director of Aspect Medical Systems, Inc., a medical technology company, until its acquisition by Covidien PLC in 2009. Mr. Kania holds a degree in physics from Dartmouth College and an MBA from Harvard Business School.

Connie Mack, III has served as a director since June 2001. Since January 2010, Mr. Mack has been a partner and senior policy advisor for Liberty Partners Group, a public policy consulting firm, and since January 2007, Mr. Mack has been a partner and senior policy advisor of Liberty Partners of Florida, LLC, a public policy consulting firm. From February 2005 to December 2009, Mr. Mack served as senior policy advisor at King & Spalding LLP, an international law firm. From February 2001 to February 2005, Mr. Mack served as a senior policy advisor at Shaw Pittman LLP, an international law firm. Mr. Mack was first elected to public office as a U.S. Congressman for the 13th district in the State of Florida in 1982. In 1988, he was elected to a six-year term in the U.S. Senate from the State of Florida and was re-elected for a second term in 1994. He did not seek re-election in 2000. Mr. Mack was the Republican Conference Secretary from 1995 to 1997. He was Chairman of the Senate Republican Conference from 1997 to 2001 and Chairman of the Joint Economic Committee from 1999 to 2001. Mr. Mack is also a director of Darden Restaurants Inc., a full service restaurant company, Genzyme Corporation, a global biotechnology company, Moody's Corporation, a company that provides credit ratings, related research and other products and services, and Mutual of America Life Insurance Company, a company that provides pension and retirement-related products and services. Mr. Mack holds a BS in Business Administration from the University of Florida.

Katherine Napier has served as a director since April 2009. Ms. Napier has served as the Chief Executive Officer of Arbonne International, a skin care and cosmetics company, since October 2009. Ms. Napier is a 20-year veteran of Procter & Gamble, a Fortune 500 company that manufactures and distributes a broad range of consumer products, where from 1979 to 2002, she rose from assistant brand manager to vice president and general manager of the company's North American pharmaceutical business. Ms. Napier also served as senior vice president of marketing at McDonald's Corporation, where she led the company's reinvigoration of its business with women and families. She received her bachelor's degree in economics and studio fine arts from Georgetown University and earned a master of business administration degree in marketing and finance from Xavier University. Ms. Napier serves on the board of directors of the Alberto Culver Company, a beauty products company, Catholic Health Care Partners, a not-for-profit health care system, Hill-Rom Holdings, Inc., a science-based aesthetic products company, Xavier University, and the board of visitors of Wake Forest University Calloway School of Business. She was a director of Mentor Corporation, a hospital and health care equipment company, before its acquisition by Johnson & Johnson in 2009 and of Third Wave Technologies, Inc., a molecular diagnostics company, until its acquisition by Hologic Inc. in 2008.

Lance Willsey, MD has served as a director since May 2000. Dr. Willsey was a founding partner of DCF Capital, a hedge fund focused on investing in the life sciences, from July 1998 to April 2002. From July 1997 to July 1998, Dr. Willsey served on the Staff Department of Urologic Oncology at Dana Farber Cancer Institute at Harvard University School of Medicine. From July 1996 to July 1997, Dr. Willsey served on the Staff Department of Urology at Massachusetts General Hospital at Harvard University School of Medicine, where he was also a urology resident from July 1992 to July 1996. Dr. Willsey is also a director of Exelixis, Inc. Dr. Willsey holds a BS in physiology from Michigan State University and an MS in biology and an MD from Wayne State University.

Patrick J. Zenner has served as a director since March 2003 and as chairman of our Board of Directors since April 2008. From July 2007 until March 2008, Mr. Zenner served as our interim Chief Executive Officer. In January 2001, Mr. Zenner retired from Hoffmann-La Roche Inc., North America, the prescription drug unit of the Roche Group, a leading research-based health care enterprise, where he served as President and Chief Executive Officer since 1993. Mr. Zenner joined Hoffman-La Roche Inc. in 1969 and held a number of domestic and international management positions at the company prior to becoming Chief Executive Officer in 1993. Mr. Zenner also serves as a director of ArQule, Inc., a clinical-stage biotechnology company, Geron Corporation, a biopharmaceutical company, West Pharmaceutical Services, Inc., a medical device company, and Xoma Ltd., a biopharmaceutical company. He was a director of CuraGen Corporation, a clinical-stage biopharmaceutical company, until its acquisition by Celldex Therapeutics, Inc. in 2009. Mr. Zenner also served as interim Chief Executive Officer of CuraGen Corporation from May 2005 to March 2006. Mr. Zenner holds a BS in business administration from Creighton University and an MBA from Fairleigh Dickinson University and is a trustee of both universities.

* * *

A majority of our Board members have served multiple terms over several years. 2009 was a transformational year for our Company during which a number of important events occurred that we believe position us for future success: (1) we completed a significant transaction with Genzyme Corporation that generated cash we are using to develop our business,

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(2) we hired a new President and Chief Executive Officer, (3) we hired a new Chief Financial Officer, (4) we hired a new Chief Science Officer; (5) we relocated our headquarters and operations from Boston, Massachusetts to Madison, Wisconsin; and (6) we sharply re-focused our business on the development of a stool-based DNA colorectal cancer screening product and seeking FDA clearance of that product. In light of these changes and the new opportunities and challenges ahead, the Corporate Governance and Nominating Committee is in the process of assessing the composition of our Board and is beginning to interview prospective new Board candidates. If our Board composition is changed as a result of this process, it is anticipated that new directors would be appointed by the Board, in accordance with applicable Delaware law and the Company's bylaws, based on the recommendations of our Nominating and Corporate Governance Committee.

Executive Officers

Kevin T. Conroy is discussed above under the caption "Directors."

Maneesh K. Arora has served as our Senior Vice President and Chief Financial Officer since April 2009. Mr. Arora served as chief financial officer of Third Wave Technologies, Inc., a molecular diagnostics company, from January 2006 until the acquisition of Third Wave Technologies, Inc. by Hologic, Inc. in July 2008. He joined Third Wave Technologies, Inc. in January 2003 as director of strategy and was promoted successively to vice president and senior vice president in 2004. Prior to joining Third Wave Technologies, Inc., Mr. Arora was director of corporate strategy for Nalco Chemical Company, a water treatment and process improvement company. He began his career at Kraft Foods, a food company, as a financial analyst and held several positions of increasing responsibility during his nine years there. He earned a bachelor's degree in economics from the University of Chicago and a master of business administration degree from the Kellogg Graduate School of Management.

Graham P. Lidgard, Ph.D. was appointed Senior Vice President, Chief Science Officer of the Company in August 2009. Dr. Lidgard joined us from Nanogen Inc., a medical diagnostics products company, where he was Senior Vice President of research and development from 2003 to 2009. Dr. Lidgard led the research and development organization at Gen-Probe Inc., a molecular diagnostics company, which developed that company's Procleix blood screening products and Aptima sexually transmitted disease products. Dr. Lidgard also created and led the system development group at Gen-Probe that developed its fully automated Tigris system. Prior to joining Gen-Probe in 1995, Dr. Lidgard was co-founder and Vice President of product development of Matritech Inc., a Cambridge, Massachusetts-based developer of diagnostic products for the early detection of bladder cancer. Before he co-founded Matritech, Dr. Lidgard held senior positions at Ciba Corning Diagnostics Corp.'s worldwide diagnostics group. While at Ciba Corning, he was involved in the development of more than 70 510(k)-cleared products. He led the program for the development of the magnetic particle chemiluminescent technology that became the ACS:180 and Centaur systems. Dr. Lidgard earned a Bachelor's degree with honors and a Doctorate in biological chemistry from the University of Manchester in England.

Barry M. Berger, MD joined the Company in 1999 and was appointed Senior Vice President, Chief Medical Officer of the Company in August 2009. He received his medical degree from the University of Pennsylvania. Dr. Berger held a faculty appointment at Harvard Medical School and has been affiliated staff in Pathology at Brigham and Women's Hospital since 1982. His post-graduate training includes a post-doctoral fellowship in immunology (University of Pennsylvania), medical internship at Boston University Hospital, and Residency/Chief Resident in Pathology at Brigham and Women's Hospital in Boston, MA. Dr. Berger is boarded in Anatomic, Clinical and Cytologic pathology. Earlier in his career, Dr. Berger spent 11 years as the Director of the Department of Pathology and Laboratory Medicine of Harvard Pilgrim Healthcare. He is the past chairman of the Advisory Committee on Clinical Laboratories for the Commonwealth of MA and formerly served on the Economics Committee of the American College of Medical Genetics. He currently serves on the Executive Committee of the Massachusetts Society of Pathologists and the Health Policy Task Group of the National Colorectal Cancer Roundtable.

**CERTAIN UNITED STATES FEDERAL INCOME AND ESTATE TAX CONSIDERATIONS
FOR NON-U.S. HOLDERS**

The following discussion summarizes certain material U.S. federal income and estate tax considerations relating to the acquisition, ownership and disposition of our common stock purchased in this offering by a non-U.S. holder (as defined below). This discussion is based on the provisions of the Internal Revenue Code of 1986, as amended, final, temporary and proposed U.S. Treasury regulations promulgated thereunder and current administrative rulings and judicial decisions, all as in effect as of

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the date hereof. All of these authorities may be subject to differing interpretations or repealed, revoked or modified, possibly with retroactive effect, which could materially alter the tax consequences to non-U.S. holders described in this prospectus.

There can be no assurance that the IRS will not take a contrary position to the tax consequences described herein or that such position will not be sustained by a court. No ruling from the IRS has been obtained with respect to the U.S. federal income or estate tax consequences to a non-U.S. holder of the purchase, ownership or disposition of our common stock.

This discussion is for general information only and is not tax advice. All prospective non-U.S. holders of our common stock should consult their own tax advisors with respect to the U.S. federal, state, local and non-U.S. tax consequences of the purchase, ownership and disposition of our common stock.

As used in this discussion, the term "non-U.S. holder" means a beneficial owner of our common stock that is not any of the following for U.S. federal income tax purposes:

an individual who is a citizen or a resident of the United States;

a corporation or other entity taxable as a corporation for U.S. federal income tax purposes that was created or organized in or under the laws of the United States, any state thereof or the District of Columbia;

an estate whose income is subject to U.S. federal income taxation regardless of its source;

a trust (a) if a U.S. court is able to exercise primary supervision over the trust's administration and one or more U.S. persons have the authority to control all of the trust's substantial decisions or (b) that has a valid election in effect under applicable U.S. Treasury regulations to be treated as a U.S. person; or

an entity that is disregarded as separate from its owner for U.S. federal income tax purposes if all of its interests are owned by a single person described above.

An individual may be treated, for U.S. federal income tax purposes, as a resident of the United States in any calendar year by being present in the United States on at least 31 days in that calendar year and for an aggregate of at least 183 days during a three-year period ending in the current calendar year. The 183-day test is determined by counting all of the days the individual is treated as being present in the current year, one-third of such days in the immediately preceding year and one-sixth of such days in the second preceding year. Residents are subject to U.S. federal income tax as if they were U.S. citizens.

This discussion assumes that a prospective non-U.S. holder will hold shares of our common stock as a capital asset (generally, property held for investment). This discussion does not address all aspects of U.S. federal income and estate taxation that may be relevant to a particular non-U.S. holder in light of that non-U.S. holder's individual circumstances. In addition, this discussion does not address any aspect of U.S. federal alternative minimum, U.S. state or U.S. local or non-U.S. taxes, or the special tax rules applicable to particular non-U.S. holders, such as:

insurance companies and financial institutions;

tax-exempt organizations;

partnerships or other pass-through entities;

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regulated investment companies or real estate investment trusts;

pension plans;

persons who received our common stock as compensation;

brokers and dealers in securities;

owners that hold our common stock as part of a straddle, hedge, conversion transaction, synthetic security or other integrated investment; and

former citizens or residents of the United States subject to tax as expatriates.

If a partnership or other entity treated as a partnership for U.S. federal income tax purposes is an owner of our common stock, the treatment of a partner in the partnership generally will depend on the status of the partner and the activities of the partnership. We urge any owner of our common stock that is a partnership and partners in that partnership to consult their tax advisors regarding the U.S. federal income tax consequences of acquiring, owning and disposing of our common stock.

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Distributions on Our Common Stock

Any distribution on our common stock paid to non-U.S. holders will generally constitute a dividend for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. Distributions in excess of our current and accumulated earnings and profits will generally constitute a return of capital to the extent of the non-U.S. holder's adjusted tax basis in our common stock, and will be applied against and reduce the non-U.S. holder's adjusted tax basis. Any remaining excess will be treated as capital gain, subject to the tax treatment described below under the caption "Gain on Sale, Exchange or Other Disposition of Our Common Stock."

Dividends paid to a non-U.S. holder that are not treated as effectively connected with the non-U.S. holder's conduct of a trade or business in the United States generally will be subject to withholding of U.S. federal income tax at a rate of 30% on the gross amount paid, unless the non-U.S. holder is entitled to an exemption from or reduced rate of withholding under an applicable income tax treaty. In order to claim the benefit of a tax treaty, a non-U.S. holder must provide a properly executed IRS Form W-8BEN (or successor form) prior to the payment of dividends. A non-U.S. holder eligible for a reduced rate of withholding pursuant to an income tax treaty may be eligible to obtain a refund of any excess amounts withheld by timely filing an appropriate claim for a refund with the IRS.

Dividends paid to a non-U.S. holder that are treated as effectively connected with a trade or business conducted by the non-U.S. holder within the United States (and, if an applicable income tax treaty so provides, are also attributable to a permanent establishment or a fixed base maintained within the United States by the non-U.S. holder) are generally exempt from the 30% withholding tax if the non-U.S. holder satisfies applicable certification and disclosure requirements. To obtain the exemption, a non-U.S. holder must provide us with a properly executed IRS Form W-8ECI (or successor form) prior to the payment of the dividend. Dividends received by a non-U.S. holder that are treated as effectively connected with a U.S. trade or business generally are subject to U.S. federal income tax at rates applicable to U.S. persons. A non-U.S. holder that is a corporation may, under certain circumstances, be subject to an additional "branch profits tax" imposed at a rate of 30%, or such lower rate as specified by an applicable income tax treaty between the United States and such holder's country of residence.

A non-U.S. holder who provides us with an IRS Form W-8BEN, Form W-8ECI or other form must update the form or submit a new form, as applicable, if there is a change in circumstances that makes any information on such form incorrect.

Gain on Sale, Exchange or Other Disposition of Our Common Stock

In general, a non-U.S. holder will not be subject to any U.S. federal income tax or withholding on any gain realized from the non-U.S. holder's sale, exchange or other disposition of shares of our common stock unless:

the gain is effectively connected with a U.S. trade or business (and, if an applicable income tax treaty so provides, is also attributable to a permanent establishment or a fixed base maintained within the United States by the non-U.S. holder), in which case the gain will be taxed on a net income basis generally in the same manner as if the non-U.S. holder were a U.S. person, and, if the non-U.S. holder is a corporation, the additional branch profits tax described above in "Distributions on Our Common Stock" may also apply;

the non-U.S. holder is an individual who is present in the United States for 183 days or more in the taxable year of the disposition and certain other conditions are met, in which case the non-U.S. holder will be subject to a 30% tax on the net gain derived from the disposition, which may be offset by U.S.-source capital losses of the non-U.S. holder, if any; or

we are, or have been at any time during the five-year period preceding such disposition (or the non-U.S. holder's holding period, if shorter), a "United States real property holding corporation."

Generally, we will be a "United States real property holding corporation" if the fair market value of our U.S. real property interests equals or exceeds 50% of the sum of the fair market values of our worldwide real property interests and other assets used or held for use in a trade or business, all as determined under applicable U.S. Treasury regulations. We believe that we have not been and are not currently, and do not anticipate becoming in the future, a "United States real property holding corporation" for U.S. federal income tax purposes.

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Backup Withholding and Information Reporting

We must report annually to the IRS and to each non-U.S. holder the amount of distributions paid to such holder and the amount of tax withheld, if any. Copies of the information returns filed with the IRS to report the distributions and withholding may also be made available to the tax authorities in a country in which the non-U.S. holder is a resident under the provisions of an applicable income tax treaty or agreement.

The United States imposes a backup withholding tax on the gross amount of dividends and certain other types of payments. Dividends paid to a non-U.S. holder will not be subject to backup withholding if proper certification of foreign status (usually on IRS Form W-8BEN) is provided, and we do not have actual knowledge or reason to know that the non-U.S. holder is a U.S. person. In addition, no backup withholding or information reporting will be required regarding the proceeds of a disposition of our common stock made by a non-U.S. holder within the United States or conducted through certain U.S. financial intermediaries if the payor receives the certification of foreign status described in the preceding sentence and the payor does not have actual knowledge or reason to know that such non-U.S. holder is a U.S. person or the non-U.S. holder otherwise establishes an exemption. Non-U.S. holders should consult their own tax advisors regarding the application of the information reporting and backup withholding rules to them.

Backup withholding is not an additional tax. Amounts withheld under the backup withholding rules from a payment to a non-U.S. holder can be refunded or credited against the non-U.S. holder's U.S. federal income tax liability, if any, provided that certain required information is furnished to the IRS in a timely manner.

Recently-Enacted Legislation Relating to Foreign Accounts

Legislation has been recently enacted that imposes significant certification, information reporting and other requirements, and in certain cases, withholding taxes, on certain types of payments made to "foreign financial institutions" and certain other non-U.S. entities. The legislation is generally effective for payments made after December 31, 2012. The failure to comply with the certification, information reporting and other specified requirements in the legislation would result in withholding tax being imposed on payments of dividends and sales proceeds to foreign intermediaries and certain non-U.S. holders. Non-U.S. holders should consult their own tax advisers regarding the application of this legislation to them.

U.S. Federal Estate Tax

An individual non-U.S. holder who is treated as the owner, or who has made certain lifetime transfers, of an interest in our common stock will be required to include the value of the common stock in his or her gross estate for U.S. federal estate tax purposes and may be subject to U.S. federal estate tax, unless an applicable estate tax treaty provides otherwise or no U.S. federal estate tax is in effect.

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Under an underwriting agreement, dated April , 2010, we have agreed to sell to the underwriter named below the indicated number of our common shares.

Underwriter	Number of Shares
Robert W. Baird & Co. Incorporated	3,500,000
Total	3,500,000

The underwriting agreement provides that the underwriter is obligated to purchase all the shares of our common stock in the offering if any are purchased, other than those shares covered by the over-allotment option we describe below.

Over-Allotment Option

We have granted to the underwriter a 30-day option to purchase up to 525,000 additional shares from us at the public offering price less the underwriting discount. The option may be exercised only to cover any over-allotments of our common stock.

Offering Price

The underwriter proposes to offer the shares of our common stock initially at the public offering price on the cover page of this prospectus supplement and to selling group members at that price less a selling concession not to exceed \$ per share.

Commissions and Expenses

The underwriter and selling group members may allow a concession not to exceed \$ per share on sales to other broker/dealers. After the offering, the representatives may change the public offering price and concession and discount to broker/dealers. As used in this section:

The underwriter is a securities broker/dealer that is a party to the underwriting agreement and will have a contractual commitment to purchase shares of our common stock from us.

Selling group members are securities broker/dealers to whom the underwriter may sell shares of our common stock at the public offering price less the selling concession above, but who do not have a contractual commitment to purchase shares from us.

Broker/dealers are firms registered under applicable securities laws to sell securities to the public.

The syndicate consists of the underwriters and the selling group members.

The following table summarizes the compensation to be paid to the underwriter:

	Per Share	Without Over-Allotment	Total With Over-Allotment
Underwriting discount	\$	\$	\$

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The compensation we will pay to the underwriter will consist solely of the underwriting discount, which will be an amount equal to the offering price per share to the public of the common stock, less the amount paid by the underwriter to us per share of common stock. In accordance with the underwriting agreement, the underwriter will pay the fees of a financial advisor to the Company in connection with the offering. The underwriter has not received and will not receive from us any other item of compensation or expense in connection with this offering that would constitute underwriting compensation, in accordance with the Financial Industry Regulatory Authority's rule of fair price. The underwriter's compensation was determined through arms' length negotiations between us and the underwriter.

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We estimate the expenses payable by us in connection with this offering, other than the underwriting discount referred to above, will be approximately \$175,000. Expenses include printing, legal, accounting and transfer agent fees, and other miscellaneous fees and expenses.

NASDAQ Capital Market Listing

Our common stock is listed on the NASDAQ Capital Market under the symbol "EXAS." We cannot assure you that prices at which our shares trade in the public market after this offering will not be lower than the public offering price.

Lock-Up Agreements

We and our directors, executive officers and certain investment funds affiliated with one of our directors have agreed not to offer, sell, transfer, pledge or contract to sell, transfer or pledge any shares of our common stock or securities convertible into or exchangeable or exercisable for any of shares of our common stock without the prior written consent of Robert W. Baird & Co. Incorporated for a period of 90 days after the date of this prospectus supplement, except that these restrictions will not apply to our ability to grant equity incentive awards under the terms of equity incentive plans in effect on the date of this prospectus supplement or to issue our common stock upon any exercise of options or warrants outstanding on the date of this prospectus supplement. The restrictions will also not apply to transfers by our directors and executive officers by gift, will or intestacy so long as the transferee agrees not to make further transfers of the shares during the 90-day period.

Indemnity

We have agreed to indemnify the underwriter against liabilities under the Securities Act or to contribute to payments that the underwriter may be required to make in that respect.

Stabilization

The underwriter may engage in over-allotment transactions, stabilizing transactions and syndicate covering transactions in accordance with Regulation M under the Exchange Act.

Over-allotment transactions involve sales by the underwriter of shares in excess of the number of shares the underwriter is obligated to purchase, which creates a syndicate short position.

Stabilizing transactions permit bids to purchase shares of our common stock so long as the stabilizing bids do not exceed a specified maximum.

Syndicate covering transactions involve purchases of our common stock in the open market after the distribution has been completed to cover syndicate short positions.

These stabilizing transactions and syndicate covering transactions may cause the price of our common stock to be higher than the price that might otherwise exist in the open market. These transactions may be effected on the NASDAQ Capital Market or otherwise and, if commenced, may be discontinued at any time.

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NOTICE TO INVESTORS

Notice to Prospective Investors in the European Economic Area

In relation to each Member State, or Relevant Member State, of the European Economic Area that has implemented the Prospectus Directive, the underwriter has represented and agreed that, with effect from and including the date, or the Relevant Implementation Date, on which the Prospectus Directive is implemented in that Relevant Member State, it has not made and will not make an offer of the common stock to the public in that Relevant Member State prior to the publication of a prospectus in relation to such common stock that has been approved by the competent authority in that Relevant Member State or, where appropriate, approved in another Relevant Member State and notified to the competent authority in that Relevant Member State, all in accordance with the Prospectus Directive, except that it may, with effect from and including the Relevant Implementation Date, make an offer of the common stock to the public in that Relevant Member State at any time:

- (a) to legal entities that are authorized or regulated to operate in the financial markets or, if not so authorized or regulated, whose corporate purpose is solely to invest in securities;
- (b) to any legal entity that has two or more of (1) an average of at least 250 employees during the last financial year; (2) a total balance sheet of more than 43,000,000 and (3) an annual net turnover of more than 50,000,000, as shown in its last annual or consolidated accounts;
- (c) to fewer than 100 natural or legal persons (other than qualified investors as defined in the Prospectus Directive) subject to obtaining the prior consent of the underwriter; or
- (d) in any other circumstances which do not require the publication by us of a prospectus pursuant to Article 3 of the Prospectus Directive,

provided that no such offer of the common stock referred to in (a) to (d) above shall require us or the underwriter to publish a prospectus pursuant to Article 3 of the Prospective Directive.

For the purposes of this provision, the expression an "offer of the common stock to the public" in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and the shares of common stock to be offered so as to enable an investor to decide to purchase or subscribe the common stock, as the same may be varied in that Member State by any measure implementing the Prospectus Directive in that Member State and the expression "Prospectus Directive" means Directive 2003/71/EC and includes any relevant implementing measure in each Relevant Member State.

Notice to Prospective Investors in the United Kingdom

The underwriter has represented and agreed that:

- (a) it has only communicated or caused to be communicated and will only communicate or cause to be communicated an invitation or inducement to engage in investment activity (within the meaning of Section 21 of the Financial Services and Markets Act 2000, or FSMA) received by it in connection with the issue or sale of the common stock in circumstances in which Section 21(1) of the FSMA does not apply to Exact Sciences Corporation; and
- (b) it has complied and will comply with all applicable provisions of the FSMA with respect to anything done by it in relation to the common stock in, from or otherwise involving the United Kingdom.

LEGAL MATTERS

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K&L Gates LLP, Raleigh, North Carolina, will pass upon certain legal matters relating to this offering. Reinhart Boerner Van Deuren s.c., Milwaukee, Wisconsin, will pass upon certain legal matters relating to this offering for the underwriter.

EXPERTS

The consolidated financial statements as of and for the year ended December 31, 2009, incorporated in this prospectus supplement by reference from the Company's Annual Report on Form 10-K for the year ended December 31, 2009, and the effectiveness of the Company's internal control over financial reporting, have been audited by Grant Thornton LLP, an

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independent registered public accounting firm, as stated in their reports, which are incorporated herein by reference, upon authority of said firm as experts in accounting and auditing in giving said reports.

The consolidated financial statements of the Company as of and for each of the two years in the period ended December 31, 2008 appearing in the Company's Annual Report (Form 10-K) for the year ended December 31, 2009 have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their report thereon, included therein, and incorporated herein by reference. Such consolidated financial statements are incorporated herein by reference in reliance upon such report given on the authority of such firm as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We are currently subject to the information requirements of the Exchange Act and in accordance therewith file periodic reports, proxy statements and other information with the SEC. We also filed a registration statement on Form S-3, including exhibits, under the Securities Act, with respect to the securities offered by this prospectus supplement. This prospectus supplement and the accompanying prospectus are a part of the registration statement, but do not contain all of the information included in the registration statement or the exhibits. You may read and copy the registration statement and any other document that we file at the SEC's public reference room at 100 F Street, N.E., Washington D.C. 20549. You can call the SEC at 1-800-SEC-0330 for further information on the operation of the public reference room. You can also find our public filings with the SEC on the internet at a web site maintained by the SEC located at <http://www.sec.gov>.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to "incorporate by reference" information into this prospectus supplement and the accompanying prospectus, which means that we can disclose important information about us by referring you to another document filed separately with the SEC. The information incorporated by reference is considered to be a part of this prospectus supplement and the accompanying prospectus. We incorporate by reference the documents and reports listed below:

our Annual Report on Form 10-K for the fiscal year ended December 31, 2009, filed with the SEC on March 12, 2010; and

all documents filed after the date of this prospectus supplement and prior to the termination of the offering hereunder pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934.

Information in this prospectus supplement supersedes related information in the documents listed above, and information in subsequently filed documents supersedes related information in each of this prospectus supplement, the prospectus and the incorporated documents.

We will promptly provide, without charge to you, upon written or oral request, a copy of any or all of the documents incorporated by reference in this prospectus supplement or the prospectus, other than exhibits to those documents, unless the exhibits are specifically incorporated by reference in those documents. Requests should be directed to:

Corporate Secretary
Exact Sciences Corporation
441 Charmany Drive
Madison, Wisconsin 53719
(608) 284-5700

You can also find these filings on our website at www.exactsciences.com. We are not incorporating the information on our website other than these filings into this prospectus supplement or the prospectus.

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PROSPECTUS

EXACT SCIENCES CORPORATION

\$50,000,000

**Common Stock
Preferred Stock
Subordinated Debt Securities
Senior Debt Securities
Warrants**

**Offered by
EXACT Sciences Corporation**

100,000 Shares of Common Stock

**Offered by the
Selling Stockholder**

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 a total public offering price of \$50,000,000 on terms to be determined at the time of sale. We will provide specific terms of these securities in supplements to this prospectus.

Up to 100,000 shares of common stock may be sold from time to time in one or more offerings by the selling stockholder identified on page 18. We will not receive any proceeds from sales of shares of our common stock by the selling stockholder.

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 those securities.

Our common stock is traded on The NASDAQ Global Market under the symbol "EXAS."

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 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 3 of this prospectus. We may include additional 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 passed upon the adequacy or accuracy of this prospectus or any accompanying prospectus supplement. Any representation

to the contrary is a criminal offense.

The date of this prospectus is December 3, 2007.

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YOU SHOULD RELY ONLY ON THE INFORMATION CONTAINED IN THIS PROSPECTUS, ANY PROSPECTUS SUPPLEMENT OR ANY DOCUMENT 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. This prospectus provides you with a general description of the securities we may offer. Each time we or the selling stockholder sells securities, we will provide a prospectus supplement that will contain specific information about the securities being offered and the terms of that offering. The selling stockholder referred to in this prospectus and identified in supplements to this prospectus may offer and sell shares of our common stock under this prospectus. We will not receive any of the proceeds from any sale of shares by the selling stockholder.

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," "our" and similar names refer to EXACT Sciences Corporation and its subsidiaries.

ABOUT EXACT SCIENCES CORPORATION

EXACT Sciences Corporation is an applied genomics company that develops proprietary DNA-based technologies for use in the detection of cancer. We have selected colorectal cancer as the first application of our technologies. We have licensed certain of our patents, on an exclusive basis through December 2010, to Laboratory Corporation of America® Holdings, or LabCorp®, in connection with a commercial testing service developed by LabCorp and sold since August 2003 under the name PreGen-Plus . Our license agreement with LabCorp and LabCorp's sales of PreGen-Plus represent our primary source of revenue.

PreGen-Plus is a non-invasive stool-based DNA testing service for the detection of colorectal cancer in the average-risk population. Colorectal cancer is the second leading cause of cancer death in the U.S. and the leading cause of cancer death among non-smokers. Patients who are diagnosed early in the progression of the disease, however, are more likely to have a complete recovery and to utilize lower levels of expensive medical resources. Accordingly, the American Cancer Society recommends that all persons age 50 and above undergo regular colorectal cancer screening. Of the more than 87 million people in the United States for whom colorectal cancer screening is recommended, approximately one-half have never been screened, and a significant portion of the balance have been inadequately screened. We believe that this large population of unscreened and inadequately screened people represents an opportunity to reduce the mortality associated with colorectal cancer.

CORPORATE INFORMATION

We were incorporated in Delaware in on February 10, 1995 as Lapidus Medical System, 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

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number is (508) 683-1200. We maintain EXACT Sciences Securities Corporation, a Massachusetts securities corporation, to hold our short term investments. Our Internet website address is <http://www.exactsciences.com>. The information contained on our website is not part of this prospectus. Our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as well as reports relating to our securities filed by others pursuant to Section 16 of such act, are available through the investor relations page of our Internet website free of charge as soon as reasonably practicable after we electronically file such material with, or furnish it to, the Securities and Exchange Commission (the "SEC"). The SEC maintains an Internet website that contains reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC. The address of that website is <http://www.sec.gov>.

RISK FACTORS

Investing in our securities involves risk. 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 heading "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 heading "Risk Factors" included in our most recent annual report on Form 10-K, as revised or supplemented by our most recent quarterly report on Form 10-Q, each of which are on file with the SEC and are incorporated herein by reference, 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) contain statements with respect to the Company which constitute "forward-looking statements" within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, and are intended to be covered by the "safe harbor" created by those sections. Forward-looking statements, which are based on certain assumptions and reflect our plans, estimates and beliefs, can generally 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. Our actual results could differ materially from those discussed in the forward-looking statements. Factors that could cause or contribute to these differences include those discussed in "Risk Factors" in any prospectus supplement and in the documents incorporated by reference herein or therein.

We caution readers not to place undue reliance upon any such forward-looking statements, which speak only as of the date they are made. We disclaim any obligation, except as specifically required by law and the rules of the SEC, to publicly update or revise any such statements to reflect any change in company expectations or in events, conditions or circumstances on which any such statements may be based, or that may affect the likelihood that actual results will differ from those set forth in the forward-looking statements.

You should read this prospectus and any accompanying prospectus supplement and the documents that we reference herein and therein and have filed as exhibits to the registration statement, of which this prospectus is part, completely and with the understanding that our actual future results may be materially different from what we expect. You should assume that the information appearing in this prospectus and any accompanying prospectus supplement is accurate as of the date on the front cover of this prospectus or such prospectus supplement only. Our business, financial condition, results of operations and prospects

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may change. We may not update these forward-looking statements, even though our situation may change in the future, unless we have obligations under the Federal securities laws to update and disclose material developments related to previously disclosed information. We qualify all of the information presented in this prospectus and any accompanying prospectus supplement, and particularly our forward-looking statements, by these cautionary statements.

USE OF PROCEEDS

We currently intend to use the estimated net proceeds from the sale of these securities for working capital and other general corporate purposes, and possibly acquisitions of other companies, products or technologies. Working capital and other general corporate purposes may include research and development expenditures, capital expenditures and any other purpose that we may specify in any prospectus supplement. While we have no current plans for any specific acquisitions at this time, we believe opportunities may exist from time to time to expand our current business through strategic alliances or acquisitions with other companies, products or technologies. We have not yet determined the amount of net proceeds to be used specifically for any of the foregoing purposes. Accordingly, our management will have significant discretion and flexibility in applying the net proceeds from the sale of these securities. Pending any use, as described above, we intend to invest the net proceeds in high-quality, short-term, interest-bearing securities. Our plans to use the estimated net proceeds from the sale of these securities may change, and if they do, we will update this information in a prospectus supplement.

We will not receive any proceeds from any sales of shares of our common stock by the selling stockholder.

RATIO OF EARNINGS TO FIXED CHARGES

The following table sets forth our ratio of earnings to fixed charges for each of the periods indicated:

	NINE MONTHS ENDED					
	SEPTEMBER 30, 2007	2006	2005	2004	2003	2002
RATIO OF EARNINGS TO FIXED CHARGES	(1)	(1)	(1)	(1)	(1)	(1)
RATIO OF EARNINGS TO COMBINED FIXED CHARGES AND PREFERRED STOCK DIVIDENDS	(2)	(2)	(2)	(2)	(2)	(2)

(1) During each of these periods, our earnings were less than our fixed charges. The amount of such deficiency was approximately \$7.9 million for the nine months ended September 30, 2007, and \$12.9 million, \$14.5 million, \$18.5 million, \$28.3 million and \$29.9 million for fiscal years ended December 31, 2006, 2005, 2004, 2003 and 2002, respectively.

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

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DESCRIPTION OF CAPITAL STOCK

The following description of our common stock, together with the additional information included in any applicable prospectus supplement, summarizes the material terms and provisions of these securities but is not complete. For the complete terms of our common stock, please refer to our Sixth Amended and Restated Certificate of Incorporation, as amended to date, which we refer to as our Certificate of Incorporation, and our Amended and Restated By-laws, which we refer to as our By-laws, each of which is incorporated by reference into the registration statement of which this prospectus is a part.

General

We will describe in a prospectus supplement the specific terms of any common stock or preferred stock 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, par value \$0.01 per share and 5,000,000 shares of preferred stock, par value \$0.01 per share. The authorized and unissued shares of common stock and the authorized and undesignated shares of 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

As of November 14, 2007, there were approximately 27,075,523 shares of common stock outstanding. Holders of our common stock are entitled to one vote for each share of common stock held of record for the election of directors and on all matters submitted to a vote of stockholders. Holders of our common stock are entitled to receive dividends ratably, if any, as may be declared by our board of directors out of legally available funds, subject to any preferential dividend rights of any preferred stock then outstanding. Upon our dissolution, liquidation or winding up, holders of our common stock are entitled to share ratably in our net assets legally available after the payment of all our debts and other liabilities, subject to the preferential rights of any preferred stock then outstanding. Holders of our common stock have no preemptive, subscription, redemption or conversion rights. The rights, preferences and privileges of holders of common stock are subject to, and may be adversely affected by, the rights of the holders of shares of any series of preferred stock that we may designate and issue in the future. Except as described below in "Certain Provisions of Delaware Law and Our Certificate of Incorporation and By-laws," a majority vote of common stockholders is generally required to take action under our Certificate of Incorporation and By-laws.

Our common stock is listed on The NASDAQ Global Market under the symbol "EXAS." The American Stock Transfer and Trust Company is the transfer agent and registrar for our common stock. Its address is 59 Maiden Lane, Plaza Level, New York, NY 10038, and its telephone number is (800) 937-5449. The American Stock Transfer and Trust Company also maintains a website at www.amstock.com.

Preferred Stock

Our board of directors is authorized, without further vote or action by the stockholders, to issue from time to time up to an aggregate of 5,000,000 shares of preferred stock in one or more series and to fix or alter the designations, rights, preferences and privileges and any qualifications, limitations or restrictions of the shares of each such series of preferred stock, including the dividend rights, dividend rates, conversion rights, voting rights, terms of redemption including sinking fund provisions, redemption price or prices, liquidation preferences and the number of shares constituting any series or designations of such series, any or all of which may be greater than the rights of common stock. The issuance of preferred stock could

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adversely affect the voting power of holders of our common stock and the likelihood that holders of our common stock will receive dividend payments and payments upon liquidation and could have the effect of delaying, deferring or preventing a change in control.

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 of Delaware Law and 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.

We are subject to the provisions of Section 203 of the Delaware General Corporation Law. Subject to certain exceptions, Section 203 prohibits a publicly-held Delaware corporation from engaging in a "business combination" with an "interested stockholder" for a period of three years after the date of the transaction in which the person became an interested stockholder, unless the interested stockholder attained such status with the approval of the board of directors or unless the business combination is approved in a prescribed manner. A "business combination" is defined as a merger, asset sale or other transaction resulting in a financial benefit to the interested stockholder. Subject to various exceptions, an "interested stockholder" is a person who, together with affiliates and associates, owns, or within the past three years did own, 15% or more of a corporation's voting stock. This statute could prohibit or delay the accomplishment of mergers or other takeover or change in control attempts with respect to us and, accordingly, may discourage attempts to acquire us.

In addition, some provisions of our Certificate of Incorporation and By-laws may be deemed to have an anti-takeover effect and may delay, defer or prevent a tender offer or takeover attempt that a stockholder might deem to be in his or her best interest. The existence of these provisions could limit the price that investors might be willing to pay in the future for shares of our common stock. These provisions include:

Staggered Board. 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.

Stockholder Action; Special Meeting of Stockholders. Our Certificate of Incorporation provides that stockholders may not take action by written consent. Action may be taken only at a duly called annual or special meeting of stockholders. Our Certificate of Incorporation further provides that special meetings of our stockholders may be called only by the chairman of the board of directors, a majority of our directors or the president, and in no event may the stockholders call or force us to call a special meeting. Thus, without approval by the chairman, board of directors or president, stockholders may take no action between meetings.

Advance Notice Requirements for Stockholder Proposals and Director Nominations. Our By-laws provide that a stockholder seeking to bring business before an annual meeting of stockholders, or to nominate candidates for election as directors at an annual meeting of stockholders, must provide timely notice of this intention in writing. To be timely, a stockholder's notice must be delivered to or mailed and received at our principal executive offices not less than 120 days nor more than 150 days prior to the first anniversary of the date of our notice of annual meeting provided with respect to the previous year's annual meeting of stockholders. However, if no annual meeting of stockholders was held in the previous year or the date of the annual meeting of stockholders has been changed to be more than 30 calendar days before or 60 days after the anniversary date of the preceding year's annual meeting, then a proposal shall be

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received no later than the close of business on the tenth day following the date on which notice of the date of the meeting was first made. Certain informational requirements must also be satisfied in order for us to be required to include the proposal in our proxy materials. The By-laws also include a similar requirement for making nominations at special meetings and specify requirements as to the form and content of a stockholder's notice. These provisions may preclude stockholders from bringing matters before an annual meeting of stockholders or from making nominations for directors at an annual or special meeting of stockholders.

Authorized But Unissued Shares. The authorized but unissued shares of common stock and preferred stock are available for future issuance without stockholder approval, subject to certain limitations imposed by The NASDAQ Global Market. These additional shares may be utilized for a variety of corporate acquisitions and employee benefit plans. The existence of authorized but unissued and unreserved common stock and preferred stock could render more difficult or discourage an attempt to obtain control of us by means of a proxy contest, tender offer, merger or otherwise.

Super-Majority Voting. Delaware law provides generally that the affirmative vote of a majority of the shares entitled to vote on any matter is required to amend a corporation's certificate of incorporation or bylaws, unless a corporation's certificate of incorporation or bylaws, as the case may be, require a greater percentage. 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 also 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.

DESCRIPTION OF DEBT SECURITIES

We may sell the securities being offered pursuant to this prospectus directly to purchasers, to or through underwriters, through dealers or agents, or through a combination of such methods. The prospectus supplement with respect to the securities being offered will set forth the terms of the offering of those securities, including the names of the underwriters, dealers or agents, if any, the purchase price, the net proceeds to us, any underwriting discounts and other items constituting underwriters' compensation, the initial public offering price, any discounts or concessions allowed or reallocated or paid to dealers and any securities exchanges on which such securities may be listed.

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 the 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.

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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. 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 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;

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;

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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;

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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 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;

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 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, any 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.

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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.

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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 depository, or its nominee, is the registered owner of a registered global security, the depository 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 depository 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 depository 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 depository or its nominee to the depository 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 depository or its nominee; or

any other matter relating to the actions and practices of the depository, its nominee or any of its participants.

We expect that the depository, 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 depository'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.

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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.

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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

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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 indentures supplemental to the indenture, among other things:

to add guarantees to or secure any series of debt securities;

to 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;

to 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;

to 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;

to 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;

to add to or change any of the provisions of the indenture to supplement any of the provisions of the indenture in order 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;

to 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;

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

to 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.

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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

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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.

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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

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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. In the case of subordinated debt securities, the money and U.S. government obligations held in trust will not be subject to the subordination provisions of the indenture.

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, executed and delivered in form satisfactory to the trustee, 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, Employees and Stockholders

No director, officer, incorporator or stockholder of EXACT Sciences, as such, shall have any liability for any obligations of EXACT Sciences under the debt securities or the indenture or for any claim based on, in respect of, or by reason of, such obligations or their creation, solely by reason of his, her, or its status as director, officer, incorporator or stockholder of EXACT Sciences. By accepting a debt security, each holder waives and releases all such liability, but only such liability. The waiver and release are part of the consideration for issuance of the debt securities. Nevertheless, such waiver may not be effective to waive liabilities under the federal securities laws and it has been the view of the SEC that such a waiver is against public policy.

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Conversion or Exchange Rights

Any debt securities offered hereby may be convertible into or exchangeable for shares of our equity or other securities. The terms and conditions of such conversion or exchange will be set forth in the applicable prospectus supplement. Such terms may include, among others, the following:

the conversion or exchange price;

the conversion or exchange period;

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

events requiring adjustment to the conversion or exchange price; and

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

Concerning the Trustee

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

The indenture contains limitations on the right of the trustee, should it become a creditor of EXACT Sciences, to obtain payment of claims in certain cases or to realize on certain property received in respect of any such claim as security or otherwise. If the trustee acquires an interest that conflicts with any duties with respect to the debt securities, the trustee is required to either resign or eliminate such conflicting interest to the extent and in the manner provided by the indenture.

The initial trustee is one of a number of banks with which we may maintain ordinary banking relationships and with which we may maintain credit facilities.

Limitations on Issuance of Bearer Debt Securities

Debt securities in bearer form are subject to special U.S. tax requirements and may not be offered, sold, or delivered within the United States or its possessions or to a U.S. person, except in certain transactions permitted by U.S. tax regulations. Investors should consult the relevant prospectus supplement, in the event that bearer debt securities are issued for special procedures and restrictions that will apply to such an offering.

DESCRIPTION OF WARRANTS

We may issue securities warrants for the purchase of debt securities, preferred stock or common stock. Securities warrants may be issued independently or together with debt securities, preferred stock or common stock and may be attached to or separate from any offered securities. Each series of securities warrants will be issued under a separate warrant agreement to be entered into between us and a warrant agent. The

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securities warrant agent will act solely as our agent in connection with the securities warrants and will not assume any obligation or relationship of agency or trust for or with any registered holders of securities warrants or beneficial owners of securities warrants. This summary of some provisions of the securities warrants is not complete. You should refer to the securities warrant agreement, including the forms of securities warrant certificate representing the securities warrants, relating to the specific securities

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warrants being offered for the complete terms of the securities warrant agreement and the securities warrants. That securities warrant agreement, together with the terms of securities warrant certificate and securities warrants, will be filed with the SEC in connection with the offering of the specific securities warrants.

The particular terms of any issue of securities warrants will be described in the prospectus supplement relating to the issue. Those terms may include:

the title of such warrants;

the aggregate number of such warrants;

the price or prices at which such warrants will be issued;

the currency or currencies (including composite currencies) in which the price of such warrants may be payable;

the terms of the securities purchasable upon exercise of such warrants and the procedures and conditions relating to the exercise of such warrants;

the price at which the securities purchasable upon exercise of such warrants may be purchased;

the date on which the right to exercise such warrants will commence and the date on which such right shall expire;

any provisions for adjustment of the number or amount of securities receivable upon exercise of the warrants or the exercise price of the warrants;

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

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

if applicable, the date on and after which such warrants and the related securities will be separately transferable;

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

any other terms of such warrants, including terms, procedures and limitations relating to the exchange or exercise of such warrants.

The prospectus supplement relating to any warrants to purchase equity securities may also include, if applicable, a discussion of certain U.S. federal income tax and ERISA considerations.

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Securities warrants for the purchase of preferred stock and common stock will be offered and exercisable for U.S. dollars only. Securities warrants will be issued in registered form only.

Each securities warrant will entitle its holder to purchase the principal amount of debt securities or the number of shares of preferred stock or common stock at the exercise price set forth in, or calculable as set forth in, the applicable prospectus supplement.

After the close of business on the expiration date, unexercised securities warrants will become void. We will specify the place or places where, and the manner in which, securities warrants may be exercised in the applicable prospectus supplement.

Upon receipt of payment and the warrant certificate properly completed and duly executed at the corporate trust office of the warrant agent or any other office indicated in the applicable prospectus supplement, we will, as soon as practicable, forward the purchased securities. If less than all of the warrants represented by the warrant certificate are exercised, a new warrant certificate will be issued for the remaining warrants.

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Prior to the exercise of any securities warrants to purchase debt securities, preferred stock or common stock, holders of the securities warrants will not have any of the rights of holders of the debt securities, preferred stock or common stock purchasable upon exercise, including (i) in the case of securities warrants for the purchase of debt securities, the right to receive payments of principal of, any premium or interest on the debt securities purchasable upon exercise or to enforce covenants in the applicable indenture, or (ii) in the case of securities warrants for the purchase of preferred stock or common stock, the right to vote or to receive any payments of dividends on the preferred stock or common stock purchasable upon exercise.

SELLING STOCKHOLDER

The following table sets forth information about the selling stockholder's beneficial ownership of our common stock as of November 28, 2007 (such information has been provided by the selling stockholder) and after the sale of the common stock offered by the selling stockholder, assuming all such shares are sold. The selling stockholder has not committed to sell any shares under this prospectus. The number presented under "Shares of Common Stock Beneficially Owned After the Completion of the Offering" assumes that all of the shares offered by the selling stockholder are sold and that the selling stockholder acquires no additional shares of our common stock before the completion of this offering. The selling stockholder may offer all, some or none of the shares of our common stock beneficially owned by the selling stockholder. We will pay all expenses incurred with respect to the registration and sale of the common stock. The selling stockholder has not held any position or office with us or our affiliates within the last three years or has had a material relationship with us or any of our predecessors or affiliates within the past three years, other than as a result of the ownership of our shares or other securities. The percentages of shares owned are based on 27,073,440 shares of our common stock outstanding as of November 2, 2007, which includes the outstanding shares of common stock offered by this prospectus. The shares offered by this prospectus may be offered from time to time by the selling stockholder named below. The selling stockholder acquired the shares pursuant to the terms of a Manufacturing and Supply Agreement between us and the selling stockholder dated as of June 8, 2007.

Name of Selling Stockholder (1)	Shares of Common Stock Beneficially Owned Prior to the Offering		Shares of Common Stock Registered for Sale Hereby	Shares of Common Stock Beneficially Owned After the Completion of the Offering	
	Number	Percent		Number	Percent
OncoMethylome Sciences S.A. (2)	100,000	*	100,000		

*

less than 1%

(1)

Throughout this prospectus, when we refer to the "selling stockholder," we mean the person listed in the table above, as well as the pledges, donees, assignees, transferees, successors and others who later hold the selling stockholder's interests, and when we refer to the shares of our common stock being offered by this prospectus on behalf of the selling stockholder, we are referring to the shares of our common stock held by the selling stockholder.

(2)

Herman Spolders bvba, as Chief Executive Officer of OncoMethylome Sciences S.A., and Herman Spolders, as Managing Director of Herman Spolders bvba, each have voting and investment power with respect to such shares. Herman Spolders bvba and Mr. Spolders each disclaim beneficial ownership of such shares. The principal address for OncoMethylome Sciences S.A. is Tour 5 GIGA niveau +3, Av. de l'Hopital 11, 4000 Liege, Belgium.

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PLAN OF DISTRIBUTION

We and/or the selling stockholder may sell the securities being offered pursuant to this prospectus directly to purchasers, to or through underwriters, through broker-dealers or agents, or through a combination of such methods. The prospectus supplement with respect to the securities being offered will set forth the terms of the offering of those securities, including the names of the underwriters, broker-dealers or agents, if any, the purchase price, the net proceeds to us, any underwriting discounts and other items constituting underwriters' compensation, the initial public offering price, any discounts or concessions allowed or reallocated or paid to broker-dealers and any securities exchanges on which such securities may be listed.

If underwriters are used in an offering, we and/or the selling stockholder will execute an underwriting agreement with such underwriters and will specify the name of each underwriter and the terms of the transaction (including any underwriting discounts and other terms constituting compensation of the underwriters and any dealers) in a prospectus supplement. The securities may be offered to the public either through underwriting syndicates represented by managing underwriters or directly by one or more investment banking firms or others, as designated. If an underwriting syndicate is used, the managing underwriter(s) will be specified on the cover of the prospectus supplement. If underwriters are used in the sale, the offered securities will be acquired by the underwriters for their own accounts and may be resold from time to time in one or more transactions, including negotiated transactions, at a fixed public offering price or at varying prices determined at the time of sale. Any public offering price and any discounts or concessions allowed or reallocated or paid to dealers may be changed from time to time. Unless otherwise set forth in the prospectus supplement, the obligations of the underwriters to purchase the offered securities will be subject to conditions precedent and the underwriters will be obligated to purchase all of the offered securities if any are purchased.

We and/or the selling stockholder may grant to the underwriters options to purchase additional securities to cover over-allotments, if any, at the public offering price, with additional underwriting commissions or discounts, as may be set forth in a related prospectus supplement. The terms of any over-allotment option will be set forth in the prospectus supplement for those securities.

If any underwriters are involved in the offer and sale, they will be permitted to engage in transactions that maintain or otherwise affect the price of the securities. These transactions may include over-allotment transactions, purchases to cover short positions created by the underwriter in connection with the offering and the imposition of penalty bids. If an underwriter creates a short position in the securities in connection with the offering by selling more securities than set forth on the cover page of the applicable prospectus supplement, the underwriter may reduce that short position by purchasing the securities in the open market. In general, purchases of a security to reduce a short position could cause the price of the security to be higher than it might be in the absence of such purchases. As noted above, underwriters may also choose to impose penalty bids on other underwriters and/or selling group members. This means that if underwriters purchase securities on the open market to reduce their short position or to stabilize the price of the securities, they may reclaim the amount of the selling concession from those underwriters and/or selling group members who sold such securities as part of the offering.

Neither we nor any underwriter 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 such securities. In addition, neither we nor any underwriter make any representation that such underwriter will engage in such transactions or that such transactions, once commenced, will not be discontinued without notice.

If broker-dealers are used in an offering, we and/or the selling stockholder will sell the securities to the broker-dealers as principals. The broker-dealers then may resell the securities to the public at varying prices which they determine at the time of resale. The names of the broker-dealers and the terms of the transaction will be specified in a prospectus supplement. Broker-dealers engaged by the selling stockholder may arrange for other brokers-dealers to participate in sales. Broker-dealers may receive commissions or

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discounts from the selling stockholder (or, if any broker-dealer acts as agent for the purchaser of shares, from the purchaser) in amounts to be negotiated. The selling stockholder does not expect these commissions and discounts to exceed what is customary in the types of transactions involved. Any profits on the resale of shares of common stock by a broker-dealer acting as principal might be deemed to be underwriting discounts or commissions under the Securities Act of 1933, as amended, also referred to in this prospectus as the Securities Act. Discounts, concessions, commissions and similar selling expenses, if any, attributable to the sale of shares will be borne by the selling stockholder.

The securities may be sold directly by us and/or the selling stockholder or through agents we and/or the selling stockholder designate from time to time at a fixed price or prices, which may be changed, or at varying prices determined at the time of sale. If agents are used in an offering, the names of the agents and the terms of the agency will be specified in a prospectus supplement. Unless otherwise indicated in a prospectus supplement, the agents will act on a best-efforts basis for the period of their appointment.

Broker-dealers and agents named in a prospectus supplement and selling stockholders that are also broker-dealers may be deemed to be underwriters (within the meaning of the Securities Act) of the securities described therein. In addition, we and/or the selling stockholder may sell the securities directly to institutional investors or others who may be deemed to be underwriters within the meaning of the Securities Act with respect to any resales thereof.

Underwriters, dealers and agents may be entitled to indemnification by us and/or the selling stockholder against specific civil liabilities, including liabilities under the Securities Act, or to contribution with respect to payments which the underwriters or agents may be required to make in respect thereof, under underwriting or other agreements. The terms of any indemnification provisions will be set forth in a prospectus supplement. Certain underwriters, dealers or agents and their associates may engage in transactions with and perform services for us in the ordinary course of business.

If so indicated in a prospectus supplement, we and/or the selling stockholder will authorize underwriters or other persons acting as our agents to solicit offers by institutional investors to purchase securities pursuant to contracts providing for payment and delivery on a future date. We and/or the selling stockholder may enter into contracts with commercial and savings banks, insurance companies, pension funds, investment companies, educational and charitable institutions and other institutional investors. The obligations of any institutional investor will be subject to the condition that its purchase of the offered securities will not be illegal at the time of delivery. The underwriters and other agents will not be responsible for the validity or performance of such contracts.

Any common stock sold pursuant to a prospectus supplement will be eligible for quotation and trading on NASDAQ, subject to official notice of issuance. Any underwriters to whom securities are sold by us for public offering and sale may make a market in the securities, but such underwriters will not be obligated to do so and may discontinue any market making at any time without notice.

In order to comply with the securities laws of some states, if applicable, the securities offered hereby will be sold in those jurisdictions only through registered or licensed brokers or dealers. In addition, in some states securities may not be sold unless they have been registered or qualified for sale in the applicable state or an exemption from the registration or qualification requirement is available and complied with.

The selling stockholder may sell its shares pursuant to this prospectus, any prospectus supplement or pursuant to Rule 144 under the Securities Act, which permits limited resale of shares purchased in a private placement subject to the satisfaction of certain conditions, including, among other things, the availability of certain current public information concerning the issuer, the resale occurring following the required holding period under Rule 144 and the number of shares being sold during any three-month period not excluding certain limitations.

From time to time, the selling stockholder may pledge or grant a security interest in some or all of our common stock owned by the selling stockholder. If the selling stockholder defaults in the performance of

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its secured obligations, the pledgees or secured parties may offer and sell such common stock from time to time by this prospectus. The selling stockholder also may transfer and donate our common stock owned by the selling stockholder in other circumstances. The number of shares of our common stock beneficially owned by the selling stockholder will decrease as and when the selling stockholder transfers or donates its shares of our common stock or defaults in performing obligations secured by its shares of our common stock. The plan of distribution for the securities offered and sold under this prospectus will otherwise remain unchanged, except that the transferees, donees, pledgees, other secured parties or other successors in interest will be selling shareholders for purposes of this prospectus.

LEGAL MATTERS

The validity of the securities offered hereby will be passed upon for us by Goodwin Procter LLP, Boston, Massachusetts. If the securities are being distributed in an underwritten offering, certain legal matters will be passed upon for the underwriters by counsel identified in the applicable prospectus supplement.

EXPERTS

The consolidated financial statements of EXACT Sciences Corporation appearing in EXACT Sciences Corporation's Annual Report on Form 10-K for the year ended December 31, 2006 and EXACT Sciences Corporation management's assessment of the effectiveness of internal control over financial reporting as of December 31, 2006 included therein, have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their reports thereon included therein, and incorporated herein by reference. Such consolidated financial statements and management's assessment are incorporated herein by reference in reliance upon such reports given on the authority of such firm as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We are a public company and file annual, quarterly and current reports, proxy statements and other information with the Securities and Exchange Commission. You may read and copy any document we file at the SEC's Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549. You can request copies of these documents by writing to the SEC and paying a fee for the copying cost. Please call the SEC at 1-800-SEC-0330 for more information about the operation of the public reference room. Our SEC filings are also available to the public on the SEC's website at <http://www.sec.gov>, or on our website at <http://www.exactsciences.com> under the "Investor Relations" link. Information contained on our website is not part of this prospectus. In addition, our stock is listed for trading on The NASDAQ Global Market. You can read and copy reports and other information concerning us at the offices of the National Association of Securities Dealers, Inc. located at 1735 K Street, Washington, D.C. 20006.

This prospectus is only part of a Registration Statement on Form S-3 that we have filed with the SEC under the Securities Act of 1933, as amended, and therefore omits certain information contained in the Registration Statement. We have also filed exhibits and schedules with the Registration Statement that are excluded from this prospectus, and you should refer to the applicable exhibit or schedule for a complete description of any statement referring to any contract or other document. You may:

inspect a copy of this prospectus, including the exhibits and schedules, without charge at the public reference room;

obtain a copy of this prospectus from the SEC upon payment of the fees prescribed by the SEC; or

obtain a copy of this prospectus from the SEC website.

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INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE

The SEC allows us to "incorporate by reference" information from other documents that we file with them, which means that we can disclose important information in this prospectus by referring to those documents. The information incorporated by reference is considered to be part of this prospectus, and information that we file later with the SEC will automatically update and supersede the information in this prospectus. We incorporate by reference the documents listed below and any future filings made with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, as amended. The documents we are incorporating by reference as of their respective dates of filing are:

Our Annual Report on Form 10-K for the fiscal year ended December 31, 2006, filed with the SEC on March 15, 2007;

Our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2007, filed with the SEC on May 8, 2007; June 30, 2007, filed with the SEC on August 8, 2007; and September 30, 2007, filed with the SEC on November 6, 2007;

Our Current Reports on Form 8-K filed with the SEC on March 23, 2007; June 8, 2007 (Item 8.01 only); June 14, 2007; July 3, 2007; July 23, 2007; August 15, 2007; September 7, 2007; and November 21, 2007;

Portions of our Proxy Statement filed with the SEC on April 27, 2007 that have been incorporated by reference into our Annual Report on Form 10-K; and

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.

All documents and reports filed by us with the SEC pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act (other than Current Reports on Form 8-K containing only information furnished under Item 2.02 or Item 7.01 of Form 8-K, unless otherwise indicated therein) after the date of this prospectus and prior to the termination of the offering made hereby shall be deemed to be incorporated by reference into this prospectus and to be a part hereof from the date of filing of such documents. Any statement contained in a document incorporated or deemed to be incorporated by reference herein shall be deemed to be modified or superseded for purposes of this prospectus to the extent that a statement contained herein or in any other subsequently filed document which also is or is deemed to be incorporated by reference herein or in any prospectus supplement modifies or supersedes such statement. Any statement so modified or superseded shall not be deemed, except as so modified or superseded, to constitute a part of this prospectus.

We will provide, without charge to each person, including any beneficial owner, to whom this prospectus is delivered, upon written or oral request of such person, a copy of any or all of the documents incorporated herein by reference other than exhibits, unless such exhibits specifically are incorporated by reference into such documents or this document. Requests for such documents should be addressed in writing or by telephone to:

EXACT Sciences Corporation
100 Campus Drive
Marlborough, MA 01752
Attention: Charles R. Carelli, Jr., Chief Financial Officer
(508) 683-1200

You should rely only on the information contained in this prospectus, any prospectus supplement or any document 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.

3,500,000

Shares of Common Stock

Prospectus Supplement

April , 2010

Baird
