EXACT SCIENCES CORP
Form 424B5
July 23, 2015

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Filed Pursuant to Rule 424(b)(5)
Registration No. 333-205751

CALCULATION OF REGISTRATION FEE

Title of Each Class of Securities to be Registered	Amount to be Registered	Proposed Maximum Aggregate Offering Price Per Share	Proposed Maximum Aggregate Offering Price	Amount of Registration Fee(1)
Common stock	8,050,000	$25.500	$205,275,000	$23,852.96
Total Registration Fee				$23,852.96

(1) Calculated pursuant to Rule 457(r).

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PROSPECTUS SUPPLEMENT
(To Prospectus dated July 20, 2015)

7,000,000 Shares

Exact Sciences Corporation

Common Stock

We are offering 7,000,000 shares of our common stock. Our common stock is traded on the NASDAQ Capital Market under the symbol "EXAS." On July 20, 2015, the last reported sale price of our common stock on the NASDAQ Capital Market was $27.03 per share.

Investing in our common stock involves a high degree of risk. Please read "Risk Factors" beginning on page S-8 of this prospectus supplement, on page 3 of the accompanying prospectus and in the documents incorporated by reference into this prospectus supplement.

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

	PER SHARE	TOTAL
Public Offering Price	$ 25.50	$ 178,500,000.00
Underwriting Discounts and Commissions[(1)]	$ 0.50	$ 3,500,000.00
Proceeds to Exact Sciences Corporation (Before Expenses)	$ 25.00	$ 175,000,000.00

(1) The underwriters will also be reimbursed for certain expenses incurred in this offering. See "Underwriting" for details.

Delivery of the shares of common stock is expected to be made on or about July 24, 2015. We have granted the underwriters an option for a period of 30 days to purchase an additional 1,050,000 shares of our common stock. If the underwriters exercise the option in full, the total underwriting discounts and commissions payable by us will be $4,025,000 and the total proceeds to us, before expenses, will be $201,250,000.

Joint Book-Running Managers

Jefferies **Baird**

Prospectus Supplement dated July 21, 2015.

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Prospectus Supplement

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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 and its subsidiaries. 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 underwriters 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.

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CAUTIONARY STATEMENT ABOUT FORWARD-LOOKING INFORMATION

Certain information set forth in this prospectus supplement, set forth in the accompanying prospectus or incorporated by reference herein or therein, 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

We are a molecular diagnostics company currently focused on the early detection and prevention of some of the deadliest forms of cancer. We have developed an accurate, non-invasive, patient-friendly screening test for the early detection of colorectal cancer and pre-cancer, and we are currently working on the development of tests for lung cancer, pancreatic cancer and esophageal cancer.

Cologuard®

Our Cologuard test is designed to detect pre-cancerous lesions or polyps, and each of the four stages of colorectal cancer. Cologuard is a non-invasive, stool-based DNA (sDNA) screening test designed to detect DNA markers, which in published studies have been shown to be associated with colorectal cancer. In addition to DNA markers, our test includes a protein marker to detect blood in the stool utilizing an antibody-based fecal immunochemical test (FIT).

Colorectal cancer is the second leading cause of cancer deaths in the United States and the leading cause of cancer deaths among nonsmokers.

It is widely accepted that colorectal cancer is among the most preventable, yet least prevented cancers. Colorectal cancer can take up to 10-15 years to progress from a pre-cancerous lesion to metastatic cancer and death. Patients who are diagnosed early in the progression of the disease with pre-cancerous lesions or polyps, or early-stage cancer are more likely to have a complete recovery and to be treated less expensively. Accordingly, the American Cancer Society (ACS) recommends that all people age 50 and older undergo regular colorectal cancer screening. Of the more than 80 million people in the United States for whom routine colorectal cancer screening is recommended, nearly 47 percent have not been screened according to current guidelines. Poor compliance with screening guidelines has meant that nearly two-thirds of colorectal cancer diagnoses are made in the disease's late stages. The five-year survival rates for stages 3 and 4 are 67 percent and 12 percent, respectively.

We believe the large population of unscreened and inadequately screened patients represents a significant opportunity for a patient friendly screening test like ours. Pre-cancerous polyps are present in approximately 6 percent of average risk people 50 years of age and older who undergo routine colorectal cancer screening.

The competitive advantages of sDNA screening provide a significant market opportunity. Assuming a 30-percent test adoption rate and a three-year screening interval, we estimate the potential U.S. market for sDNA screening to be more than $2 billion and we estimate the potential global market opportunity to be greater than $3 billion.

Physicians and others assessing the effectiveness and value of our Cologuard test, will likely consider, among other things, Cologuard's sensitivity and specificity in identifying colorectal cancer and pre-cancerous polyps. "Sensitivity" (also called the true positive rate) measures the percentage of colorectal cancer or pre-cancerous polyps that our Cologuard test correctly identifies. "Specificity" (also called the true negative rate) measures the percentage of people who our Cologuard test correctly identifies as not having colorectal cancer or pre-cancerous polyps.

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On August 11, 2014, the U.S. Food and Drug Administration (FDA) approved Cologuard for use as the first (and currently only) sDNA noninvasive colorectal cancer screening test. Our submission to the FDA for Cologuard included the results of our pivotal DeeP-C clinical trial, which had over 10,000 patients enrolled at 90 enrollment sites in the U.S. and Canada. The results of our DeeP-C clinical trial for Cologuard were published in the New England Journal of Medicine in April 2014. The peer-reviewed study, "Multi-target Stool DNA Testing for Colorectal-Cancer Screening", highlighted the performance of Cologuard in the trial population:

- Cancer Sensitivity: 92%
- High-Grade Dysplasia Sensitivity: 69%
- Specificity: 87%

On October 9, 2014, the Centers for Medicare & Medicaid Services (CMS) issued a decision effecting national coverage for Cologuard. Medicare covers 43% of patients in the screening population for Cologuard. As outlined in the CMS's coverage decision, Medicare Part B will cover Cologuard once every three years for beneficiaries who meet all of the following criteria:

- Age 50 to 85 years
- Asymptomatic (no signs or symptoms of colorectal disease including, but not limited to, lower gastrointestinal pain, blood in stool, positive guaiac fecal occult blood test or fecal immunochemical test), and
- At average risk of developing colorectal cancer (no personal history of adenomatous polyps, colorectal cancer, or inflammatory bowel disease, including Crohn's Disease and ulcerative colitis; no family history of colorectal cancers or adenomatous polyps, familial adenomatous polyposis or hereditary nonpolyposis colorectal cancer).

In the 2015 Clinical Laboratory Fee Schedule, CMS established reimbursement for Cologuard (CPT code G0464) at $492.72. However, under the Protecting Access to Medicare Act of 2014, the basis for Cologuard's CMS reimbursement rate is expected to change, beginning in January, 2017.

We believe that it will be necessary to secure favorable coverage and reimbursement from commercial payors to achieve commercial success. We believe that third-party payors' reimbursement of Cologuard will depend on a number of factors, including payors' determination that it is: sensitive for colorectal cancer; not experimental or investigational; approved by major guidelines organizations; reliable, safe and effective; medically necessary; appropriate for the specific patient; and cost-effective.

Cologuard is currently included in the ACS colorectal cancer screening guidelines. The US Preventative Services Task Force (USPSTF) is expected to issue draft colorectal cancer screening guidelines during the second half of 2015 and final guidelines during the first half of 2016. If USPSTF assigns an "A" or "B" grade to Cologuard, then the Patient Protection and Affordable Care Act will require most private health insurance plans to begin (within one year after the new USPSTF recommendation) covering Cologuard without charging the patient any co-pay or deductible. Although we cannot provide any assurance that USPSTF will assign Cologuard an "A" or "B" grade, we believe receiving an "A" or "B" grade would increase Cologuard's insurance coverage and market adoption.

Our top priorities for 2015 include growing revenue for Cologuard, continuing to provide efficient service as order volume grows, and developing our product pipeline for future products.

We plan to grow Cologuard revenue through the continued efforts of our sales force to work with physicians and systems to adopt Cologuard for colorectal cancer screening. In addition, we are working with payors to secure favorable reimbursement for Cologuard which will be a key component to growing revenue in 2015.

Another key priority for 2015 is to achieve and maintain at least a 70% compliance rate for patients who are prescribed Cologuard and to whom we ship a Cologuard test kit. As of June 30, 2015, our patient

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compliance rate for Cologuard was approximately 73% The patient compliance rate is derived from the number of valid test results reported divided by the number of collection kits shipped to patients 60 or more days prior to June 30, 2015.

A critical part of the value proposition of Cologuard is our physician and patient engagement team which helps to drive compliance for Cologuard as the team actively engages with patients to help them get screened. This activity is focused on having patients complete Cologuard tests that have been ordered for them by their physicians and supports physicians in their efforts to have their patients screened. In addition, monthly compliance reports are provided to physicians relevant to their patient population.

Our sales and marketing strategy includes three main elements with a focus on physicians, patients and payors.

We are engaging physicians with several strategies. We have a 245 person sales team, including approximately 200 in a direct field sales force, actively engaging with physicians and their staffs to emphasize the need for colorectal cancer screening, educating them on the value of Cologuard and enrolling them in our physician ordering system to enable them to prescribe the test. We are focused on specific physicians based on specialty and propensity to prescribe colorectal cancer screening tests. We are also focused on physician groups and larger regional and national health systems. Further, to build awareness, we have launched a medical education program that includes online training and peer-to-peer presentations. Additionally, pursuant to our agreement with Ironwood Pharmaceuticals, 160 Ironwood sales representatives promote Cologuard to healthcare practitioners to whom they also promote Ironwood's LINZESS therapy for the treatment of irritable bowel syndrome with constipation and chronic idiopathic constipation.

After the launch of Cologuard, we initiated a significant public relations effort to engage patients. We have conducted targeted direct-to-patient advertising campaigns through social media, print and other channels.

One of the key components to engaging with payors was securing coverage from CMS, which we did in October of 2014. Additionally, we are providing cost effectiveness data to payors to make the case for Cologuard reimbursement. We are focusing our efforts on large national and regional insurers, states that require health insurers to cover colorectal cancer screening consistent with the ACS guidelines and health plans that have affiliated health systems.

As part of our commercialization strategy, we established a lab facility that is certified pursuant to applicable Federal Clinical Laboratory Improvement Amendments (CLIA) regulations and certain state law requirements. Our commercial lab operation is housed in a 32,000 square foot facility in Madison, Wisconsin. We have the capacity at our lab to process one million Cologuard tests per year.

Product Pipeline

We also are focused on developing our product pipeline for future products. We are continuing to collaborate with MAYO on future products related to early detection of gastrointestinal (GI) cancers specifically in the areas of esophageal and pancreatic cancers. GI cancers account for 145,000 or 25% of all U.S. cancer deaths annually and represent a significant market opportunity for future products. In February 2015, we amended and restated our license agreement with MAYO to extend our arrangement with MAYO for an additional five years and broaden our collaboration efforts to develop screening, surveillance and diagnostic tests and tools for use in connection with gastrointestinal cancers, pre-cancers, diseases and conditions.

In June 2015, we entered into a joint development and license agreement with The University of Texas MD Anderson Cancer Center to establish a collaboration aimed at developing a blood-based lung cancer screening test to determine the need for low-dose computed tomography (LDCT). This test would offer the opportunity to screen nearly 11 million Americans considered high-risk smokers and former smokers. The partnership is also aimed at developing a diagnostic test to determine the malignant status of nodules found through computed tomography screening. This test would be valuable to nearly four million Americans

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diagnosed with lung nodules each year. The American Cancer Society estimates that lung cancer will be diagnosed in 221,200 Americans and cause 158,040 deaths in the United States this year and that, world-wide, lung cancer will be diagnosed in 1,825,000 people and cause 1,590,000 deaths. Currently, more than half of lung cancer cases are diagnosed at an advanced stage, after symptoms appear, when the five-year survival rate is in the low single digits. If detected at an early stage, lung cancer's five-year survival rate can be as high as 80 percent.

Additionally, we will continue to explore opportunities for expanding the indications of Cologuard such as for patients between the ages of 40-49 or for high risk patients.

Recent Developments

In the second quarter of 2015, we completed approximately 21,000 Cologuard tests, up from 11,000 completed tests in the first quarter of 2015, and recognized $8.1 million of revenue. During the second quarter of 2015, the cumulative number of ordering physicians (physicians who ordered at least one Cologuard test) grew to more than 14,700. Additionally, as of the end of the second quarter of 2015, the patient compliance rate (calculated based on the number of valid test results reported divided by the number of collection kits shipped to patients 60 or more days prior to the measurement date) for Cologuard was approximately 73 percent, an increase from approximately 71 percent as of the end of the first quarter.

Corporate Information

Our executive offices are located at 5601 Research Park Drive, Madison, Wisconsin 53711. Our telephone number is (608) 284-5700. Our Internet website address is *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:	7,000,000 shares
Shares of common stock outstanding after the offering:	95,913,304 shares (or 96,963,304 shares if the underwriters' option to purchase additional shares is exercised in full).

Underwriters' Option to Purchase Additional Shares

We have granted the underwriters an option to purchase up to 1,050,000 additional shares of our common stock. This option is exercisable, in whole or in part, for a period of 30 days from the date of the underwriting agreement.

Use of Proceeds

We intend to use the net proceeds from this offering to fund expansion of our Cologuard commercialization activities, to fund our product development efforts, and for general corporate and working capital purposes. See "Use of Proceeds."

NASDAQ Capital Market Listing

Our common stock is listed on the NASDAQ Capital Market under the symbol "EXAS".

Risk Factors

Investing in our common stock involves a high degree of risk. 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 information contained in or incorporated by reference under "Risk Factors" beginning on page S-8 of this prospectus supplement, page 3 of the accompanying prospectus and in the documents incorporated by reference into this prospectus supplement.

Outstanding Shares

The number of shares outstanding after the offering is based on 88,913,304 shares outstanding as of March 31, 2015, and includes 55,087 shares of unvested restricted stock issued to directors. The number of outstanding shares after the offering does not include, in each case as of March 31, 2015:

- 5,221,920 shares subject to outstanding stock options at a weighted average exercise price of $4.83 per share;
- 2,249,896 shares subject to outstanding restricted stock unit awards; or
- 764,951 additional shares of common stock reserved for issuance under our equity incentive plans (or 9,124,951 additional shares, subject to stockholder approval of an amendment to our 2010 Omnibus Long-Term Incentive Plan at our 2015 annual stockholder meeting scheduled for July 23, 2015).

If the underwriters' option to purchase additional shares is exercised in full, we will issue and sell an additional 1,050,000 shares of our common stock and will have 96,963,304 shares outstanding after the offering.

Except as otherwise noted, all information in this prospectus supplement assumes no exercise of the underwriters' option to purchase additional shares.

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RISK FACTORS

We operate in a rapidly changing environment that involves a number of risks, some of which are beyond our control. This discussion highlights some of the risks which may affect future operating results. These are the risks and uncertainties we believe are most important for you to consider. 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 we may be unable to stay in business. 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.

We may never become profitable.

We have incurred losses since we were formed and have had only modest product, service and royalty fee revenues to date. From our date of inception on February 10, 1995 through December 31, 2014, we have accumulated a total deficit of approximately $420.8 million. We expect that our losses will continue for at least the next several years and that we will be required to invest significant additional funds toward development and commercialization 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 products based on our technologies will be sufficient to make us profitable.

We may need additional capital to execute our business plan.

Although we believe that we have sufficient capital to fund our operations for at least the next twelve months, we may require additional capital to fully fund the commercialization of our Cologuard test and other business expansion activities, including the development of new products and services. If we raise additional funds through the sale of equity, convertible debt or other equity-linked securities, our stockholders' ownership will be diluted. 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.

Our success depends heavily on our Cologuard colorectal cancer screening test.

For the foreseeable future, our ability to generate revenues will depend entirely on the commercial success of our Cologuard test. The commercial success of our Cologuard test and our ability to generate revenues will depend on several factors, including the following:

- acceptance in the medical community;
- inclusion of Cologuard in healthcare guidelines, such as those developed by ACS and USPSTF;
- patient acceptance of and demand for the Cologuard test;
- successful sales, marketing and educational programs;
- the number of patients tested for colorectal cancer as well as the number of patients who use Cologuard for that purpose;
- sufficient coverage and reimbursement by third party payors;
- the amount and nature of competition from other colorectal cancer or pre-cancer screening products and procedures;
- maintaining FDA marketing approval of Cologuard in the United States and the receipt and maintenance of marketing approval from foreign regulatory authorities;

- maintaining and defending patent protection for the intellectual property relevant to Cologuard; and
- our ability to establish and maintain commercial manufacturing, distribution, sales force and CLIA laboratory testing capabilities.

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If we are unable to develop substantial sales of our Cologuard test or if we are significantly delayed or limited in doing so, our business prospects would be adversely affected.

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

The market for colorectal cancer and pre-cancer screening is large, consisting of more than 80 million Americans age 50 and above. As a result, this market has attracted competitors, some of which possess significantly greater financial and other resources and development capabilities than we do. Some companies and institutions are developing serum-based tests and 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 colorectal cancer or pre-cancer. We are aware of at least four companies Epigenomics AG, Applied Proteomics, Inc., Gene News, EDP Biotech Corporation and Quest Diagnostics that are developing blood-based tests for the detection of colorectal cancer. Epigenomics AG completed a large multi-center study designed to demonstrate the performance of its blood-based screening test for colorectal cancer and submitted the results to the FDA in June 2014. It is our understanding that the FDA issued a response letter to Epigenomics AG requiring additional clinical studies to demonstrate the performance of its test and Epigenomics AG is in the process of conducting a study to satisfy the FDA's requirements. We also face competition from procedure-based detection technologies such as flexible sigmoidoscopy, colonoscopy and "virtual" colonoscopy (a radiological imaging approach which visualizes the inside of the bowel by use of spiral computerized axial tomography known as a CT scan) as well as traditional screening tests such as FOBT and FIT and newer screening technologies such as the PillCam COLON approved by FDA in February 2014. Our competitors may also be working on additional methods of detecting colorectal cancer and pre-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 or stronger business relationships.

If third-party payors, including managed care organizations, do not approve reimbursement for our Cologuard test at adequate reimbursement rates, we may be unable to successfully commercialize our Cologuard test which would likely have a material adverse effect on our business.

Successful commercialization of our Cologuard test depends, in large part, on the availability of adequate reimbursement from government insurance plans, managed care organizations and private insurance plans. Although we received a positive coverage decision and what we believe is a favorable initial reimbursement rate from the Centers for Medicare and Medicaid (CMS) for our Cologuard test, it is also critical that other third party payors approve reimbursement for our Cologuard test at adequate reimbursement rates. Third-party payors are increasingly attempting to contain healthcare costs by limiting both coverage and the level of reimbursement for new healthcare products approved for marketing by the FDA. As a result, there is significant uncertainty surrounding whether the use of tests that incorporate new technology, such as our Cologuard test, will be eligible for coverage by third-party payors or, if eligible for coverage, what the reimbursement rates will be. 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 and pre-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 decisions from third-party payors, including managed care organizations, approving reimbursement for our Cologuard test at adequate levels, its commercial success would be compromised and our revenues would be significantly limited. We may also experience material delays in obtaining such reimbursement decisions and payment for our Cologuard test which are beyond our control. Moreover, coverage determinations and reimbursement rates are subject to change, and we cannot guarantee that even if we initially achieve adequate coverage and reimbursement rates, they will be applicable to our Cologuard test in the future.

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If our clinical studies do not satisfy providers, payors, patients and others as to the reliability, effectiveness and superiority of our Cologuard test, we may experience reluctance or refusal on the part of physicians to order, and third-party payors to pay for, our test.

Although we have received FDA approval for our Cologuard test, 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 and other healthcare providers, third-party payors and patients that our Cologuard test is 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, our Cologuard test, which could prevent us from successfully commercializing it.

We have limited selling and marketing resources and lack sales, marketing, customer support, manufacturing, distribution and commercial laboratory experience, which may restrict our success in commercializing products.

To grow our business as planned, we must expand our sales, marketing and customer support capabilities, which will involve developing and administering our commercial infrastructure and/or collaborative commercial arrangements and partnerships. We must also maintain satisfactory arrangements for the manufacture and distribution of our Cologuard test. In addition, as part of our commercialization strategy, we have recently established a CLIA certified lab facility to process Cologuard tests and provide patient results. We have limited experience managing a sales force, customer support operation and operating a manufacturing operation and clinical lab facility and we may encounter difficulties retaining and managing the specialized workforce these activities require. We may seek to partner with others to assist us with any or all of these functions. However, we may be unable to find appropriate third parties with whom to enter into these arrangements. Furthermore, if we do enter into these arrangements, these third parties may not perform as expected.

If we are unable to deploy and maintain effective sales and marketing capabilities, we will have difficulty achieving market awareness and selling our products and services.

To achieve commercial success for our Cologuard test and our future products and services, we must continue to develop and grow our sales and marketing organization. We currently have a 245 person sales team, including approximately 200 in a direct field sales force. Our direct sales force calls directly on healthcare providers throughout the United States to initiate sales of our Cologuard test. Our sales organization must explain to healthcare providers the reliability, effectiveness and benefits of Cologuard as compared to existing screening methods such as FOBT and FIT. We may not be able to successfully manage our dispersed sales force. We have also entered into marketing arrangements with independent sales organizations, but we cannot be assured that they will be effective. Because of the competition for their services, we may be unable to partner with or retain additional qualified sales representatives, either as our employees or independent contractors or through independent sales organizations. Further, we may not be able to enter into agreements with sales representatives on commercially reasonable terms, if at all.

Establishing and maintaining sales and marketing capabilities will be expensive and time-consuming. Our expenses associated with maintaining our sales force may be disproportional compared to the revenues we may be able to generate on sales of the Cologuard test.

The success of our Cologuard test depends on the degree of market acceptance by physicians, patients, healthcare payors and others in the medical community.

Our Cologuard test may not gain market acceptance by physicians, healthcare payors and others in the medical community. The degree of market acceptance of our Cologuard test will depend on a number of factors, including:

- its demonstrated sensitivity and specificity for detecting colorectal cancer and pre-cancer;

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- its price;
- the availability of alternative screening methods;
- the willingness of physicians to prescribe Cologuard;
- the interval at which patients are screened using Cologuard; and
- sufficient third-party coverage or reimbursement.

Even if our Cologuard test is superior to other colorectal cancer screening options, adequate third-party reimbursement is obtained and medical practitioners choose to order our Cologuard test, 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, approximately 47 percent of these individuals are not screened according to current guidelines. Use of a stool-based DNA colorectal cancer screening test will require people to collect a stool sample, which some people may be reluctant to do. If our Cologuard test does not achieve an adequate level of acceptance, we may not generate material revenues and we may not become profitable.

Our assumptions regarding the market opportunity for Cologuard may not prove true. We estimate the potential market opportunity for Cologuard assuming, among other things, a 30-percent test adoption rate and a three-year screening interval. Although ACS guidelines recommend a three-year screening interval and CMS has determined that Medicare will cover the test at this interval, physicians, healthcare payors, the FDA and other regulators and opinion leaders could recommend a less frequent testing schedule. Further, patients may not comply with the recommended testing interval.

The US Preventative Services Task Force (USPSTF) is expected to issue draft colorectal cancer screening guidelines during the second half of 2015 and final guidelines during the first half of 2016. If USPSTF assigns an "A" or "B" grade to Cologuard, then the Patient Protection and Affordable Care Act will require most private health insurance plans to begin (within one plan year after the new USPSTF recommendation) covering Cologuard without charging the patient any co-pay or deductible. We believe that the grade which USPSTF assigns to Cologuard could significantly affect the market acceptance of our Cologuard test. We cannot provide any assurance that USPSTF will assign Cologuard a positive grade. If USPSTF provides a grade lower than a "B", healthcare professionals may be less likely to recommend Cologuard and healthcare payor coverage of Cologuard could decrease, which could materially and negatively impact our financial results and prospects.

We expect to make significant investments to research and develop new cancer diagnostic tools, which may not be successful.

In addition to commercializing our Cologuard test, we are focused on developing our pipeline for future products, including screening and diagnostic tests for lung cancer, pancreatic cancer and esophageal cancer. Our efforts to develop new cancer diagnostic tools or other products or services may not be successful, may cause us to incur significant expense and may distract our management from successfully commercializing Cologuard. Any new cancer diagnostic tools we develop will be subject to clinical trials and FDA approval, which may be a lengthy and expensive process. There can be no guarantee that we will develop any products that the FDA would approve or that would be commercially viable. If we determine that any of our current or future development programs is unlikely to succeed, we may abandon it without any return on our investment into the program.

We may not be able to successfully establish and maintain collaborative and licensing arrangements, which could adversely affect our ability to develop and commercialize our Cologuard test and any other products and services.

The development and commercialization of our Cologuard test and any other products and services relies, directly or indirectly, upon strategic collaborations and licensing agreements with third parties. We currently

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have collaborative and licensing arrangements with MAYO Foundation for Medical Education and Research and MD Anderson. In addition, we have licensing agreements with Hologic and MDx Health. Such arrangements provide us with intellectual property crucial to our product development, including technology that we have incorporated into our Cologuard test. Our dependence on licensing, collaboration and other similar agreements with third parties may subject us to a number of risks. 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 and will not be breached or terminated early. Nor can there be any assurance that we will be able to enter into the relationships necessary to successfully commercialize our Cologuard test or any other product or service we may develop. Any failure to obtain or retain the rights to necessary technologies could require us to re-configure our products and services, which could negatively impact their commercial sale or increase the associated costs, either of which could materially harm our business and adversely affect our future revenues.

As we seek to commercialize and market our Cologuard test and develop new products and services, we expect to continue and expand our reliance on collaborative and licensing arrangements. Establishing new strategic collaborations and licensing arrangements is difficult and time-consuming. Discussions with potential collaborators or licensors may not lead to the establishment of collaborations on favorable terms, if at all. To the extent we agree to work exclusively with one collaborator in a given area, our opportunities to collaborate with other entities could be limited. Potential collaborators or licensors may reject collaborations with us based upon their assessment of our financial, regulatory or intellectual property position. Even if we successfully establish new collaborations, these relationships may never result in the successful commercialization of our Cologuard test or any other product or service.

Even though our Cologuard test has received regulatory clearance in the United States, if we do not receive regulatory clearance for Cologuard in other jurisdictions, our prospects may be materially and negatively affected.

Governments in countries outside the United States also regulate diagnostic tests marketed in such countries, and obtaining their approvals can be lengthy, expensive and highly uncertain. The approval process varies from country to country and the requirements governing the conduct of clinical trials, pricing and reimbursement vary greatly from country to country. In certain jurisdictions, we are required to finalize operational, reimbursement, price approval and funding processes prior to marketing our Cologuard test. We may not receive regulatory approval for our Cologuard test in countries other than the United States on a timely basis, if ever. Even if approval is granted in any such country, the approval may require limitations on the uses or availability of our Cologuard test. Failure to obtain regulatory approval for our Cologuard test in territories outside the United States could have a material adverse effect on our business prospects.

We face uncertainty related to healthcare reform, pricing, coverage and reimbursement, which could reduce our revenue.

Recent healthcare reform laws, including the Patient Protection and Affordable Care Act and the Protecting Access to Medicare Act of 2014 ("PAMA"), are significantly affecting the U.S. healthcare and medical services industry. Existing legislation, and possible future legal and regulatory changes, could substantially change the structure and finances of the health insurance system and the methodology for reimbursing medical services, drugs and devices, including our current and future products and services. Any change in reimbursement policy could result in a change in patient co-payments, which could adversely affect patient willingness and ability to use our Cologuard test and any other product or service we may develop. Healthcare reforms, which may intend to reduce healthcare costs, may have the effect of discouraging third-party payors from covering certain kinds of medical products and services, particularly newly developed technologies, such as our Cologuard test.

Even without further legislative reform, there can be no assurance that CMS will maintain its current reimbursement rate for our Cologuard test. If the CMS reimbursement rate for Cologuard is reduced, our

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revenues could be adversely affected. There can be no assurance that CMS and third party payors who initially decide to cover Cologuard will continue to cover Cologuard. A hedge fund has submitted a request that CMS reconsider its reimbursement rate for Cologuard, which was presented at a CMS public meeting on July 16, 2015. We can provide no assurance that CMS will not negatively alter its coverage or reimbursement rate based on this request or otherwise.

Under PAMA, the basis for Cologuard's CMS reimbursement rate is expected to change, beginning in January, 2017. Under PAMA, we expect the CMS reimbursement rate for Cologuard to be tied to the volume-weighted median reimbursement for Cologuard from commercial payors. Therefore, if Cologuard's volume-weighted median commercial reimbursement rate falls below the current CMS reimbursement rate (or the adjusted rate, if CMS determines to adjust the reimbursement rate as a result of the above-referenced request for reconsideration or otherwise) in 2016, we anticipate that the CMS reimbursement rate would decline in 2017.

If we fail to meet any applicable requirements of CLIA or similar state laws, that failure could adversely affect any future payor consideration of our technologies, prevent their approval entirely, and/or interrupt the commercial sale of any products and services and otherwise cause us to incur significant expense.

We are subject to federal and state laws and regulations regarding the operation of clinical laboratories. Federal Clinical Laboratory Improvement Amendments (CLIA) requirements and laws of certain states impose certification requirements for clinical laboratories, and establish standards for quality assurance and quality control, among other things. Clinical laboratories are subject to inspection by regulators, and to sanctions for failing to comply with applicable requirements. Sanctions available under CLIA include prohibiting a laboratory from running tests, requiring a laboratory to implement a corrective plan, and imposing civil monetary penalties. If we fail to meet any applicable requirements of CLIA or state law, that failure could adversely affect any future payor consideration of our technologies, prevent their approval entirely, and/or interrupt the commercial sale of any products and services and otherwise cause us to incur significant expense.

We currently perform our Cologuard test predominantly in one laboratory facility. If this or any future facility or our equipment were damaged or destroyed, or if we experience a significant disruption in our operations for any reason, our ability to continue to operate our business could be materially harmed.

We currently perform our Cologuard test predominantly in a single laboratory facility in Madison, Wisconsin. Our headquarters and manufacturing facilities are also located in Madison, Wisconsin. If these, or any future facilities, were to be damaged, destroyed or otherwise unable to operate, whether due to fire, floods, storms, tornadoes, other inclement weather events or natural disasters, employee malfeasance, terrorist acts, power outages, or otherwise, our business could be severely disrupted. If our Madison, Wisconsin, laboratory is disrupted, we may not be able to perform our Cologuard test or generate test reports as promptly as patients and healthcare providers require or expect, or possibly not at all. If we are unable to perform our Cologuard test or generate test reports within a timeframe that meets patient and healthcare provider expectations, our business, financial results and reputation could be materially harmed.

We currently maintain insurance against damage to our property and equipment and against business interruption and research and development restoration expenses, subject to deductibles and other limitations. If we have underestimated our insurance needs with respect to an interruption, or if an interruption is not subject to coverage under our insurance policies, we may not be able to cover our losses.

Failure in our information technology, storage systems or our clinical laboratory equipment could significantly disrupt our operations and our research and development efforts, which could adversely impact our revenues, as well as our research, development and commercialization efforts.

Our ability to execute our business strategy depends, in part, on the continued and uninterrupted performance of our information technology, or IT, systems, which support our operations, including at our

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clinical laboratory, and our research and development efforts. We are substantially dependent on our IT systems to receive and process Cologuard test orders, securely store patient health records and deliver the results of our Cologuard tests. IT systems are vulnerable to damage from a variety of sources, including telecommunications or network failures, malicious human acts and natural disasters. Moreover, despite network security and back-up measures, some of our servers are potentially vulnerable to physical or electronic break-ins, computer viruses and similar disruptive problems. Despite the precautionary measures we have taken to prevent unanticipated problems that could affect our IT systems, sustained or repeated system failures that interrupt our ability to generate and maintain data, and in particular to operate our clinical laboratory, could adversely affect our ability to operate our business. Any interruption in the operation of IT systems could have an adverse effect on our operations.

We rely on courier delivery services to transport Cologuard collection kits to patients and samples back to our laboratory facility for analysis. If these delivery services are disrupted, customer satisfaction and our business could be negatively impacted.

We ship Cologuard collection kits to patients, and patients ship samples to our Madison, Wisconsin, laboratory facility for analysis, by air and ground express courier delivery service. Disruptions in delivery service, whether due to bad weather, natural disaster, terrorist acts or threats, or for other reasons, can adversely affect customer satisfaction, specimen quality and our ability to provide our services on a timely basis.

We may be subject to substantial costs and liability, or be prevented from using technologies incorporated in our Cologuard test, as a result of litigation or other proceedings relating to patent or other intellectual property 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 pre-cancer and is designed to maximize our patent protection against third parties in the United States and, potentially, in certain foreign countries. We have filed patent applications that we believe cover the methods we have designed and use in our Cologuard test to detect colorectal cancer and pre-cancer. In order to protect or enforce our patent and other intellectual property rights, we may have to initiate actions against third parties. Any actions regarding patents could be costly and time-consuming and divert the attention of 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, we have no way of knowing if others may have filed patent applications covering technologies 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. From time to time we have received correspondence from third parties alleging to hold intellectual property rights that could block our commercialization of products. While none of these inquiries to date have had any material effect on us, and while we do not believe that any pending correspondence would have such an effect, we may receive inquiries in the future that could have a material effect on our business. 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 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 only be available on unacceptable 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 effect on our business, financial condition and results of operations.

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Also, patents and patent 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 any competitive advantage we may otherwise have.

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, third parties may be able to compete more effectively against us and we may incur substantial litigation costs in our attempts to recover or restrict use of our intellectual property. Additionally, the U.S. Congress recently passed the Leahy-Smith America Invents Act, or the America Invents Act, which was signed into law in September 2011. The America Invents Act reforms United States patent law in part by changing the standard for patent approval from a "first to invent" standard to a "first to file" standard and developing a post-grant review system. This new legislation changes United States patent law in a way that may weaken our ability to obtain or maintain patent protection for future inventions in the United States.

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 any 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 been in the past, and may be in the future, the subject of opposition proceedings relating to our patents. We cannot guarantee you that we will be successful in defending challenges made against our patents and patent applications. Any successful third-party challenge to our patents could result in co-ownership of such patents with the 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 may adversely impact our ability to obtain new patents and facilitate third-party challenges to our existing patents.

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 our Cologuard test is 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, including independent sales representatives, 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 our products and services in certain jurisdictions.

Healthcare policy has been a subject of extensive discussion in the executive and legislative branches of the federal and many state governments and healthcare laws and regulations are subject to change. Development of the existing commercialization strategy for our Cologuard test 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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Our business is subject to various complex laws and regulations. We could be subject to significant fines and penalties if we fail to comply with these regulations.

As a provider of clinical diagnostic products and services, we are subject to extensive and frequently changing federal, state and local laws and regulations governing various aspects of our business. In particular, the clinical laboratory industry is subject to significant governmental certification and licensing regulations, as well as federal and state laws regarding:

- test ordering and billing practices;
- marketing, sales and pricing practices;
- health information privacy and security, including the Health Insurance Portability and Accountability Act of 1996, or HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and comparable state laws;
- insurance;
- anti-markup legislation; and
- consumer protection.

We are also required to comply with FDA regulations, including with respect to our labeling and promotion activities. In addition, advertising of our tests is subject to regulation by the Federal Trade Commission, or FTC. Violation of any FDA requirement could result in enforcement actions, such as seizures, injunctions, civil penalties and criminal prosecutions, and violation of any FTC requirement could result in injunctions and other associated remedies, all of which could have a material adverse effect on our business. Most states also have similar regulatory and enforcement authority for devices. Additionally, most foreign countries have authorities comparable to the FDA and processes for obtaining marketing approvals. Obtaining and maintaining these approvals, and complying with all laws and regulations, may subject us to similar risks and delays as those we could experience under FDA and FTC regulation. We incur various costs in complying and overseeing compliance with these laws and regulations.

If we fail to comply with these laws and regulations, we could incur significant fines and penalties and our reputation and prospects could suffer.

Some of our activities may subject us to risks under federal and state laws prohibiting 'kickbacks' and false or fraudulent claims.

In addition to FDA marketing restrictions, several other types of state and federal healthcare fraud and abuse laws have been applied in recent years to restrict certain marketing practices in the healthcare product and service industry and to regulate billing practices and financial relationships with physicians, hospitals and other healthcare providers. These laws include a federal law commonly known as the Medicare/Medicaid anti-kickback law, and several similar state laws, which prohibit payments intended to induce physicians or others either to refer patients or to acquire or arrange for or recommend the acquisition of healthcare products or services. While the federal law applies only to referrals, products or services for which payment may be made by a federal healthcare program, state laws often apply regardless of whether federal funds may be involved. These laws constrain the sales, marketing and other promotional activities of manufacturers of medical devices and providers of laboratory services by limiting the kinds of financial arrangements, including sales programs that may be used with hospitals, physicians, laboratories and other potential purchasers or prescribers of medical devices and laboratory services. Other federal and state laws generally prohibit individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other third-party payors that are false or fraudulent, or are for items or services that were not provided as claimed. Anti-kickback and false claims laws prescribe civil and criminal penalties (including fines) for noncompliance that can be substantial. While we continually strive to comply with these complex requirements, interpretations of the applicability of these laws to marketing and billing practices is constantly evolving and even an unsuccessful challenge could cause adverse publicity and be costly to respond to, and thus could harm our business and prospects. Our failure

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to comply with applicable laws could result in various adverse consequences which could have a material adverse effect upon our business, including the exclusion of our products and services from government programs and the imposition of civil or criminal sanctions.

The success of our business is substantially dependent upon the efforts of our senior management team.

Our success depends largely on the skills, experience and performance of key members of our senior management team including Kevin Conroy, our President and Chief Executive Officer, Maneesh Arora, our Senior Vice President and Chief Operating Officer, and Dr. Graham Lidgard, our Senior Vice President and Chief Science Officer. These executives are critical to directing and managing our growth and development in the future. Our success is substantially dependent upon our senior management's ability to lead our company, implement successful corporate strategies and initiatives, develop key relationships, including relationships with collaborators and business partners, and successfully commercialize products and services in the United States and abroad. While our management team has significant experience in securing FDA approvals for diagnostic products, we have considerably less experience in commercializing a product or service. The efforts of our management team will be critical to us as we develop our technologies and seek to commercialize our Cologuard test and other FDA approved products and services.

Our success depends on our ability to retain our managerial personnel and to attract additional personnel.

Our success depends in large part on our ability to attract and retain managerial personnel. If we were to lose any of our senior management team, we may experience difficulties in competing effectively, developing our technologies and implementing our business strategies. Competition for desirable personnel is intense, and there can be no assurance that we will be able to attract and retain the necessary staff. The failure to maintain management or to attract sales personnel as we commercialize our Cologuard test could materially adversely affect our business, financial condition and results of operations.

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

The sale and use of our Cologuard test could lead to product or professional liability claims based on allegations that one of our products contained a design or manufacturing defect or our laboratory was negligent in processing test results, which resulted in the failure to detect the disease for which it was designed or an unnecessary procedure which caused harm. A product or professional 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 liability insurance would protect our assets from the financial impact of defending a liability claim. Any claim brought against us, with or without merit, could increase our liability insurance rates or prevent us from securing insurance coverage in the future.

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

We do not have the ability to independently conduct the clinical or other studies that will be required to obtain FDA approval for future products we may develop or the approval of foreign regulatory bodies that may be required for such future products as well as our Cologuard test. 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. These third-party contractors may not complete activities on schedule or conduct studies in accordance with regulatory requirements or our study design. Our reliance on third parties that we do not control will 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 may prepare and comply 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

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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 a required regulatory approval.

Delaware law, our charter documents and rights agreement could impede or discourage a takeover or change of control that stockholders may consider favorable.

As a Delaware corporation, we are subject to certain anti-takeover provisions. Under Delaware law, a corporation may not engage in a business combination with any holder of 15% or more of its capital stock unless the holder has held the stock for three years or, among other things, the board of directors has approved the transaction. Accordingly, our board of directors could rely on Delaware law to prevent or delay an acquisition of our company. In addition, certain provisions of our certificate of incorporation and bylaws may have the effect of delaying or preventing a change of control or changes in our management. These provisions include the following:

- Our board of directors is divided into three classes serving staggered three-year terms.
- Only our board of directors can fill vacancies on the board.
- Our stockholders may not act by written consent.
- There are various limitations on persons authorized to call a special meeting of stockholders and advance notice requirements for stockholders to make nominations of candidates for election as directors or to bring matters before an annual meeting of stockholders.
- Our board of directors may issue, without stockholder approval, shares of undesignated preferred stock.

These types of provisions could make it more difficult for a third party to acquire control of us, even if the acquisition would be beneficial to our stockholders.

In addition, in February 2011, we adopted a rights agreement that provides that in the event of (i) an acquisition of 15% or more of our outstanding common stock or (ii) an announcement of an intention to make a tender offer or exchange offer for 15% or more of our outstanding common stock, our stockholders, other than the potential acquiror, shall be granted rights enabling them to purchase additional shares of our common stock at a substantial discount to the then prevailing market price. The rights agreement could significantly dilute such acquiror's ownership position in our shares, thereby making a takeover prohibitively expensive and encouraging such acquiror to negotiate with our board of directors. Therefore, the rights agreement could make it more difficult for a third party to acquire control of us without the approval of our board of directors.

Our inability to manage growth could harm our business.

In connection with launching the commercialization of our Cologuard test, we have added, and expect to continue to add, additional personnel in the areas of sales and marketing, laboratory operations, billing and collections, quality assurance and compliance. Our number of full time employees has increased from 102, as of December 31, 2013, to 555, as of June 30, 2015. Further, as we build our commercialization efforts and expand research and development activities for new products, the scope and complexity of our operations is increasing significantly. As a result of our growth, our operating expenses and capital requirements have also increased, and we expect will continue to increase, significantly. Our ability to manage our growth effectively requires us to forecast expenses accurately and to expend funds to improve our operational, financial and management controls, reporting systems and procedures. As we move forward in commercializing our Cologuard test, we will also need to effectively manage our manufacturing, laboratory operations and sales and marketing needs, which represent new areas of oversight for us. If we are unable to manage our anticipated growth effectively, our business could be harmed.

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Our growing international operations could subject us to risks and expenses that could adversely impact the business and results of operations.

We expect to increase the availability of our Cologuard test in non-U.S. markets and to expand our operations in foreign countries. Our international expansion exposes us to risks from the failure to comply with foreign laws and regulations that differ from those under which we operate in the U.S., as well as U.S. rules and regulations that govern foreign activities such as the U.S. Foreign Corrupt Practices Act. In addition, we may be adversely affected by other risks associated with operating in foreign countries. Economic uncertainty in some of the geographic regions in which we operate, including developing regions, could result in the disruption of commerce and negatively impact cash flows from our operations in those areas.

Risks inherent in our international operations include:

- numerous and varied non-U.S. regulatory requirements, including with respect to healthcare, that are subject to change and that could limit our ability to offer or market our Cologuard test or other products and services we may develop on acceptable terms, if at all;
- numerous and varied U.S. regulatory requirements, including import- and export-related laws and regulations and the U.S. Foreign Corrupt Practices Act;
- changes by foreign governments and other foreign healthcare payors in reimbursement rates for our Cologuard test or other products and services we may develop;
- differing local preferences and expectations for healthcare services;
- differing private and public health insurance systems, including differing approaches to coverage determinations and reimbursement amounts;
- foreign currency exchange controls and tax rates;
- foreign currency exchange rate fluctuations, including devaluations;
- potential changes in regional and local economic conditions, including local inflationary pressures;
- political instability and actual or anticipated military or political conflicts;
- difficulty in establishing, staffing and managing non-U.S. operations
- differing labor regulations;
- potential changes in or interpretations of tax laws;
- minimal protection of intellectual and other property rights in certain jurisdictions;

- varying enforcement of contractual rights in certain jurisdictions; and

- restrictive governmental actions such as those on transfer or repatriation of funds and trade protection matters, as well as the potential nationalization or seizure of business enterprises or assets.

These and other factors may have a material adverse effect on our international operations and, consequently, on our financial condition and results of operations.

We may engage in acquisitions that could disrupt our business, cause dilution to our stockholders and reduce our financial resources.

In the future, we may enter into transactions to acquire other businesses, products, services or technologies. Because we have not made any acquisitions to date, our ability to do so successfully is unproven. If we do identify suitable candidates, we may not be able to make such acquisitions on favorable terms or at all. Any acquisitions we make may not strengthen our competitive position, and these transactions may be viewed negatively by investors, healthcare providers, patients and others. We may decide to incur debt in connection with an acquisition or issue our common stock or other securities to the stockholders of the acquired company, which would reduce the percentage ownership of our existing stockholders. We could incur losses resulting from undiscovered liabilities of the acquired business that are not covered by any indemnification we may obtain from the seller. In addition, we may not be able to successfully integrate the

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acquired personnel, technologies and operations into our existing business in an effective, timely and non-disruptive manner. Acquisitions may also divert management from day-to-day responsibilities, increase our expenses and reduce our cash available for operations and other uses. We cannot predict the number, timing or size of future acquisitions or the effect that any such transactions might have on our operating results.

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. Further, sharp drops in the market price of our common stock may expose us to securities class-action litigation. Such litigation could result in substantial expenses and diversion of management's attention and corporate resources, which would seriously harm our business, financial condition and results of operations. Because we are a company with no significant operating revenue, any of the risk factors listed in this "Item 1A. Risk Factors" may be deemed material and may affect our stock price.

You will experience immediate and substantial dilution in the book value per share of the common stock you purchase.

Because the price per share of our common stock being offered may be higher than the book value per share of our common stock, you may suffer substantial dilution in the net tangible book value of the common stock you purchase in this offering. See the section entitled "Dilution" below for a more detailed discussion of the dilution you will incur if you purchase common stock in this offering. In addition, we have a significant number of options and restricted stock outstanding. If the holders of these securities exercise or convert them or become vested in them, as applicable, you may incur further dilution.

Management will have broad discretion as to the use of the proceeds from this offering, and we may not use the proceeds effectively.

Because we have not designated the amount of net proceeds received by us from this offering to be used for any particular purpose, our management will have broad discretion as to the application of the net proceeds from this offering and could use them for purposes other than those contemplated at the time of the offering. Our management may use the net proceeds for corporate purposes that may not improve our financial condition or market value.

Sales of a significant number of shares of our common stock in the public markets could depress the market price of our common stock.

Sales of a substantial number of shares of our common stock or other equity-related securities in the public markets could depress the market price of our common stock and impair our ability to raise capital through the sale of additional equity securities. We cannot predict the effect that future sales of our common stock or other equity-related securities would have on the market price of our common stock.

We have never paid cash dividends and do not intend to do so.

We have never declared or paid cash dividends on our common stock. We currently plan to retain any earnings to finance the growth of our business rather than to pay cash dividends. Payments of any cash dividends in the future will depend on our financial condition, results of operations and capital requirements, as well as other factors deemed relevant by our board of directors.

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USE OF PROCEEDS

We estimate that our net proceeds from the sale of our common stock in this offering will be approximately $174.0 million, after deducting the underwriting discount and estimated offering expenses payable by us. If the underwriters exercise in full their option to purchase additional shares, we estimate that our net proceeds from the sale of our common stock in this offering will be approximately $200.3 million, after deducting the underwriting discount and estimated offering expenses payable by us.

We intend to use the net proceeds from this offering to fund expansion of our Cologuard commercialization activities, to fund our product development efforts, and for general corporate and working capital purposes.

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.

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

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DILUTION

Our net tangible book value as of March 31, 2015, was $258.2 million, or $2.90 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 March 31, 2015. After giving effect to our sale of 7.0 million shares of common stock in this offering at the public offering price of $25.50 per share, and after deduction of the underwriters' fees and estimated offering expenses payable by us, our net tangible book value as of March 31, 2015, would have been $432.2 million, or $4.51 per share. This represents an immediate increase in net tangible book value of $1.61 per share to existing stockholders and an immediate dilution in net tangible book value of $20.99 per share to purchasers of common stock in this offering. The following table illustrates this calculation.

Public offering price per share of common stock		$ 25.50
Net tangible book value per share as of March 31, 2015	$ 2.90	
Increase per share attributable to this offering	$ 1.61	
As adjusted net tangible book value per share after this offering		$ 4.51
Dilution per share to new investors in this offering		$ 20.99

If the underwriters exercise their option to purchase additional shares in full, our as adjusted net tangible book value per share at March 31, 2015, after giving effect to this offering, would have been $4.73 per share, and the dilution to purchasers in this offering would have been $20.77 per share.

The number of shares outstanding after the offering is based on 88,913,304 shares outstanding as of March 31, 2015, and includes 55,087 shares of unvested restricted stock issued to directors. The number of outstanding shares after the offering does not include, in each case as of March 31, 2015:

- 5,221,920 shares subject to outstanding stock options at a weighted average exercise price of $4.83 per share;
- 2,249,896 shares subject to outstanding restricted stock unit awards; or
- 764,951 additional shares of common stock reserved for issuance under our equity incentive plans (or 9,124,951 additional shares, subject to stockholder approval of an amendment to our 2010 Omnibus Long-Term Incentive Plan at our 2015 annual stockholder meeting scheduled for July 23, 2015).

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MATERIAL U.S. 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 (Code), final, temporary and proposed U.S. Treasury regulations promulgated thereunder and current administrative rulings and judicial decisions, all as in effect as of 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 within the meaning of Section 1221 of the Code (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;
- regulated investment companies or real estate investment trusts;

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- 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.

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

Subject to the discussions below regarding backup withholding and the Foreign Account Tax Compliance Act, 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.

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

Subject to the discussions below regarding backup withholding and the Foreign Account Tax Compliance Act, a non-U.S. holder will generally 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" (USRPHC) 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 USRPHC for U.S. federal income tax purposes. However, because the determination of whether we are a USRPHC depends on the fair market value of our United States real property relative to the fair market value of our other business assets, there can be no assurance that we will not become a USRPHC in the future. Even if we become a USRPHC, however, as long as our common stock is regularly traded on an established securities market, such common stock will be treated as United States real property interests only if you actually or constructively hold more than five percent of such regularly traded common stock at any time during the applicable period that is specified in the Code.

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

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income tax liability, if any, provided that certain required information is furnished to the IRS in a timely manner.

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.

Recently-Enacted Legislation Relating to Foreign Accounts

In addition to the withholding described above, legislation enacted in 2010, known as the Foreign Account Tax Compliance Act ("FATCA"), generally imposes a withholding tax of 30% on dividends paid with respect to our common stock and on the gross proceeds of a sale or other disposition of our common stock, if the payments are made to a foreign entity, unless certain diligence, reporting, withholding and certification obligations and requirements are met. Subsequent U.S. Treasury regulations have delayed the implementation of withholding under FATCA with respect to dividends until after December 31, 2013, and with respect to payments of gross proceeds until after December 31, 2016.

The withholding under FATCA may be avoided if (i) the foreign entity is a "foreign financial institution" (as defined in the Code) and such institution enters into an agreement with the U.S. government to collect and provide to the U.S. tax authorities substantial information regarding U.S. account holders of such institution (which would include certain equity and debt holders of such institution, as well as certain account holders that are foreign entities with U.S. owners) or (ii) the foreign entity is not a "foreign financial institution" and makes a certification identifying its substantial U.S. owners (as defined in the Code) or makes a certification that such foreign entity does not have any substantial U.S. owners. Foreign financial institutions located in jurisdictions that have an intergovernmental agreement with the United States governing FATCA may be subject to different rules. Under certain circumstances, a non-U.S. holder of our common stock might be eligible for refunds or credits of such withholding taxes, and a non-U.S. holder might be required to file a U.S. federal income tax return to claim such refunds or credits.

Non-U.S. holders should consult their own tax advisors regarding the implications of this legislation on their investment in our common stock.

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UNDERWRITING

Subject to the terms and conditions set forth in the underwriting agreement, dated July 20, 2015, between us and Jefferies LLC and Robert W. Baird & Co. Incorporated, as the joint book-running managers, and the underwriters of this offering, we have agreed to sell to the underwriters, and each of the underwriters has agreed, severally and not jointly, to purchase from us, the respective number of shares of common stock shown opposite its name below:

Underwriter	Number of Shares
Jefferies LLC	3,500,000
Robert W. Baird & Co. Incorporated	3,500,000
Total	7,000,000

The underwriting agreement provides that the obligations of the several underwriters are subject to certain conditions precedent such as the receipt by the underwriters of officers' certificates and legal opinions and approval of certain legal matters by their counsel. The underwriting agreement provides that the underwriters will purchase all of the shares of common stock if any of them are purchased. If an underwriter defaults, the underwriting agreement provides that the purchase commitments of the nondefaulting underwriter may be increased or the underwriting agreement may be terminated. We have agreed to indemnify the underwriters and certain of their controlling persons against certain liabilities, including liabilities under the Securities Act, and to contribute to payments that the underwriters may be required to make in respect of those liabilities.

The underwriters have advised us that, following the completion of this offering, they currently intend to make a market in the common stock as permitted by applicable laws and regulations. However, the underwriters are not obligated to do so, and the underwriters may discontinue any market-making activities at any time without notice in their sole discretion. Accordingly, no assurance can be given as to the liquidity of the trading market for the common stock, that you will be able to sell any of the common stock held by you at a particular time or that the prices that you receive when you sell will be favorable.

The underwriters are offering the shares of common stock subject to their acceptance of the shares of common stock from us and subject to prior sale. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part. In addition, the underwriters have advised us that they do not intend to confirm sales to any account over which the underwriters exercise discretionary authority.

Commission and Expenses

The underwriters have agreed to purchase the shares of common stock from us at a price of $25.00 per share. The underwriters have advised us that they propose to offer the shares of common stock to the public at the public offering price set forth on the cover page of this prospectus and to certain dealers, which may include the underwriters, at that price less a concession not in excess of $0.10 per share of common stock. After the offering, the public offering price and concession to dealers may be reduced by the representatives. No such reduction will change the amount of proceeds to be received by us as set forth on the cover page of this prospectus supplement.

The following table shows the public offering price, the underwriting discounts and commissions that we are to pay the underwriters and the proceeds, before expenses, to us in connection with this offering. Such

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amounts are shown assuming both no exercise and full exercise of the underwriters' option to purchase additional shares.

	Per Share		Total	
	Without Option to Purchase Additional Shares	With Option to Purchase Additional Shares	Without Option to Purchase Additional Shares	With Option to Purchase Additional Shares
Public offering price	$ 25.50	$ 25.50	$ 178,500,000	$ 205,275,000
Underwriting discounts and commissions paid by us	$ 0.50	$ 0.50	$ 3,500,000	$ 4,025,000
Proceeds to us, before expenses	$ 25.00	$ 25.00	$ 175,000,000	$ 201,250,000

We estimate expenses payable by us in connection with this offering, other than the underwriting discounts and commissions referred to above, will be approximately $1.0 million. We also have agreed to reimburse the underwriters for up to $10,000 for their FINRA counsel fee. In accordance with FINRA Rule 5110, this reimbursed fee is deemed underwriting compensation for this offering.

Listing

Our common stock is listed on the NASDAQ Capital Market under the trading symbol "EXAS".

Option to Purchase Additional Shares

We have granted to the underwriters an option, exercisable for 30 days from the date of the underwriting agreement, to purchase, from time to time, in whole or in part, up to an aggregate of 1,050,000 shares from us at the public offering price set forth on the cover page of this prospectus supplement, less underwriting discounts and commissions. If the underwriters exercise this option, each underwriter will be obligated, subject to specified conditions, to purchase a number of additional shares proportionate to that underwriter's initial purchase commitment as indicated in the table above. This option may be exercised only if the underwriters sell more shares than the total number set forth on the cover page of this prospectus supplement.

No Sales of Similar Securities

We and our officers and directors have agreed, subject to specified exceptions, not to directly or indirectly:

- sell, offer, contract or grant any option to sell (including without limitation any short sale), pledge, transfer, establish an open "put equivalent position" within the meaning of Rule 16a-1(h) under the Exchange Act, as amended, or
- otherwise dispose of any common stock, options or warrants to acquire common stock, or securities exchangeable or exercisable for or convertible into common stock currently or hereafter owned either of record or beneficially (as defined in Rule 13d-3 under the Exchange Act, as amended), or
- publicly announce an intention to do any of the foregoing for a period of 60 days after the date of the underwriting agreement relating to this offering without the prior written consent of Jefferies LLC and Robert W. Baird & Co. Incorporated.

This restriction terminates after the close of trading of the common stock on and including the 60th day after the date of the underwriting agreement relating to this offering. However, subject to certain exceptions, in the event that either:

- during the last 17 days of the 60-day restricted period, we issue an earnings release or material news or a material event relating to us occurs, or

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- prior to the expiration of the 60-day restricted period, we announce that we will release earnings results during the 16-day period beginning on the last day of the 60-day restricted period,

then in either case the expiration of the 60-day restricted period will be extended until the expiration of the 18-day period beginning on the date of the issuance of an earnings release or the occurrence of the material news or event, as applicable, unless Jefferies LLC and Robert W. Baird & Co. Incorporated waive, in writing, such an extension.

Jefferies LLC and Robert W. Baird & Co. Incorporated may, in their sole discretion and at any time or from time to time before the termination of the 60-day period release all or any portion of the securities subject to lock-up agreements. There are no existing agreements between the underwriters and any of our shareholders who will execute a lock-up agreement, providing consent to the sale of shares prior to the expiration of the lock-up period.

Stabilization

The underwriters have advised us that they, pursuant to Regulation M under the Securities Exchange Act of 1934, as amended, certain persons participating in the offering may engage in short sale transactions, stabilizing transactions, syndicate covering transactions or the imposition of penalty bids in connection with this offering. These activities may have the effect of stabilizing or maintaining the market price of the common stock at a level above that which might otherwise prevail in the open market. Establishing short sales positions may involve either "covered" short sales or "naked" short sales.

"Covered" short sales are sales made in an amount not greater than the underwriters' option to purchase additional shares of our common stock in this offering. The underwriters may close out any covered short position by either exercising their option to purchase additional shares of our common stock or purchasing shares of our common stock in the open market. In determining the source of shares to close out the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase shares through the option to purchase additional shares.

"Naked" short sales are sales in excess of the option to purchase additional shares of our common stock. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the shares of our common stock in the open market after pricing that could adversely affect investors who purchase in this offering.

A stabilizing bid is a bid for the purchase of shares of common stock on behalf of the underwriters for the purpose of fixing or maintaining the price of the common stock. A syndicate covering transaction is the bid for or the purchase of shares of common stock on behalf of the underwriters to reduce a short position incurred by the underwriters in connection with the offering. Similar to other purchase transactions, the underwriters' purchases to cover the syndicate short sales may have the effect of raising or maintaining the market price of our common stock or preventing or retarding a decline in the market price of our common stock. As a result, the price of our common stock may be higher than the price that might otherwise exist in the open market. A penalty bid is an arrangement permitting the underwriters to reclaim the selling concession otherwise accruing to a syndicate member in connection with the offering if the common stock originally sold by such syndicate member are purchased in a syndicate covering transaction and therefore have not been effectively placed by such syndicate member.

Neither we nor any of the underwriters make any representation or prediction as to the direction or magnitude of any effect that the transactions described above may have on the price of our common stock. The underwriters are not obligated to engage in these activities and, if commenced, any of the activities may be discontinued at any time.

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

Electronic Distribution

A prospectus in electronic format may be made available by e-mail or on the web sites or through online services maintained by one or more of the underwriters or their affiliates. In those cases, prospective investors may view offering terms online and may be allowed to place orders online. The underwriters may agree with us to allocate a specific number of shares of common stock for sale to online brokerage account holders. Any such allocation for online distributions will be made by the underwriters on the same basis as other allocations. Other than the prospectus in electronic format, the information on the underwriters' web sites and any information contained in any other web site maintained by any of the underwriters is not part of this prospectus, has not been approved and/or endorsed by us or the underwriters and should not be relied upon by investors.

Other Activities and Relationships

The underwriters and certain of their affiliates are full service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, investment research, principal investment, hedging, financing and brokerage activities. The underwriters and certain of their affiliates have, from time to time, performed, and may in the future perform, various commercial and investment banking and financial advisory services for us and our affiliates, for which they received or will receive customary fees and expenses.

In the ordinary course of their various business activities, the underwriters and certain of their affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers, and such investment and securities activities may involve securities and/or instruments issued by us and our affiliates. If the underwriters or their respective affiliates have a lending relationship with us, they routinely hedge their credit exposure to us consistent with their customary risk management policies. The underwriters and their respective affiliates may hedge such exposure by entering into transactions which consist of either the purchase of credit default swaps or the creation of short positions in our securities or the securities of our affiliates, including potentially the common stock offered hereby. Any such short positions could adversely affect future trading prices of the common stock offered hereby. The underwriters and certain of their respective affiliates may also communicate independent investment recommendations, market color or trading ideas and/or publish or express independent research views in respect of such securities or instruments and may at any time hold, or recommend to clients that they acquire, long and/or short positions in such securities and instruments.

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NOTICE TO INVESTORS

Australia

This prospectus and the accompanying prospectus are not disclosure documents for the purposes of Australia's Corporations Act 2001 (Cth) of Australia, or Corporations Act, have not been lodged with the Australian Securities & Investments Commission and are only directed to the categories of exempt persons set out below. Accordingly, if you receive this prospectus supplement in Australia:

You confirm and warrant that you are either a:

- "sophisticated investor" under section 708(8)(a) or (b) of the Corporations Act;
- "sophisticated investor" under section 708(8)(c) or (d) of the Corporations Act and that you have provided an accountant's certificate to the Company which complies with the requirements of section 708(8)(c)(i) or (ii) of the Corporations Act and related regulations before the offer has been made; or
- "professional investor" within the meaning of section 708(11)(a) or (b) of the Corporations Act.

To the extent that you are unable to confirm or warrant that you are an exempt sophisticated investor or professional investor under the Corporations Act, any offer made to you under this prospectus is void and incapable of acceptance.

You warrant and agree that you will not offer any of the shares issued to you pursuant to this prospectus for resale in Australia within 12 months of those shares being issued unless any such resale offer is exempt from the requirement to issue a disclosure document under section 708 of the Corporations Act.

European Economic Area

In relation to each member state of the European Economic Area which has implemented the Prospectus Directive (each, a "Relevant Member State"), with effect from and including the date on which the Prospectus Directive is implemented in that Relevant Member State (the "Relevant Implementation Date"), no offer of any securities which are the subject of the offering contemplated by this prospectus supplement has been or will be made to the public in that Relevant Member State other than any offer where a prospectus has been or will be published in relation to such securities 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 relevant competent authority in that Relevant Member State in accordance with the Prospectus Directive, except that with effect from and including the Relevant Implementation Date, an offer of such securities may be made to the public in that Relevant Member State:

- to any legal entity which is a "qualified investor" as defined in the Prospectus Directive;
- to fewer than 100 or, if the Relevant Member State has implemented the relevant provision of the 2010 PD Amending Directive, 150, natural or legal persons (other than qualified investors as defined in the Prospectus Directive), as permitted under the Prospectus Directive, subject to obtaining the prior consent of the representatives of the underwriters for any such offer; or
- in any other circumstances falling within Article 3(2) of the Prospectus Directive;

provided that no such offer of securities shall require the Company or any of the underwriters to publish a prospectus pursuant to Article 3 of the Prospectus Directive or supplement a prospectus pursuant to Article 16 of the Prospectus Directive.

For the purposes of this provision, the expression an "offer to the public" in relation to any securities 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 securities to be offered so as to enable

an investor to decide to purchase or subscribe the securities, as the same may be varied in that Relevant Member State by any measure implementing the Prospectus Directive in that Relevant Member State and the expression "Prospectus

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Directive" means Directive 2003/71/EC (and amendments thereto, including the 2010 PD Amending Directive, to the extent implemented in the Relevant Member State), and includes any relevant implementing measure in the Relevant Member State and the expression "2010 PD Amending Directive" means Directive 2010/73/EU.

Hong Kong

No securities have been offered or sold, and no securities may be offered or sold, in Hong Kong, by means of any document, other than to persons whose ordinary business is to buy or sell shares or debentures, whether as principal or agent; or to "professional investors" as defined in the Securities and Futures Ordinance (Cap. 571) of Hong Kong and any rules made under that Ordinance; or in other circumstances which do not result in the document being a "prospectus" as defined in the Companies Ordinance (Cap. 32) of Hong Kong or which do not constitute an offer to the public within the meaning of the Companies Ordinance (Cap.32) of Hong Kong. No document, invitation or advertisement relating to the securities has been issued or may be issued or may be in the possession of any person for the purpose of issue (in each case whether in Hong Kong or elsewhere), which is directed at, or the contents of which are likely to be accessed or read by, the public of Hong Kong (except if permitted under the securities laws of Hong Kong) other than with respect to securities which are or are intended to be disposed of only to persons outside Hong Kong or only to "professional investors" as defined in the Securities and Futures Ordinance (Cap. 571) of Hong Kong and any rules made under that Ordinance.

This prospectus and the accompanying prospectus have not been registered with the Registrar of Companies in Hong Kong. Accordingly, this prospectus supplement may not be issued, circulated or distributed in Hong Kong, and the securities may not be offered for subscription to members of the public in Hong Kong. Each person acquiring the securities will be required, and is deemed by the acquisition of the securities, to confirm that he is aware of the restriction on offers of the securities described in this prospectus supplement and the relevant offering documents and that he is not acquiring, and has not been offered any securities in circumstances that contravene any such restrictions.

Japan

The offering has not been and will not be registered under the Financial Instruments and Exchange Law of Japan (Law No. 25 of 1948 of Japan, as amended), or FIEL, and the underwriters will not offer or sell any securities, directly or indirectly, in Japan or to, or for the benefit of, any resident of Japan (which term as used herein means, unless otherwise provided herein, any person resident in Japan, including any corporation or other entity organized under the laws of Japan), or to others for re-offering or resale, directly or indirectly, in Japan or to a resident of Japan, except pursuant to an exemption from the registration requirements of, and otherwise in compliance with, the FIEL and any other applicable laws, regulations and ministerial guidelines of Japan.

Singapore

This prospectus supplement and the accompanying prospectus have not been and will not be lodged or registered with the Monetary Authority of Singapore. Accordingly, this prospectus supplement and any other document or material in connection with the offer or sale, or the invitation for subscription or purchase of the securities may not be issued, circulated or distributed, nor may the securities be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to the public or any member of the public in Singapore other than (i) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore (the "SFA"), (ii) to a relevant person as defined under Section 275(2), or any person pursuant to Section 275(1A) of the SFA, and in accordance with the conditions, specified in Section 275 of the SFA, or (iii) otherwise pursuant to, and in accordance with the conditions of any other applicable provision of the SFA.

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Where the securities are subscribed or purchased under Section 275 of the SFA by a relevant person which is:

- a corporation (which is not an accredited investor as defined under Section 4A of the SFA) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or

- a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary is an accredited investor,

shares, debentures and units of shares and debentures of that corporation or the beneficiaries' rights and interest in that trust shall not be transferable for six months after that corporation or that trust has acquired the Offer Shares under Section 275 of the SFA except:

- to an institutional investor under Section 274 of the SFA or to a relevant person defined in Section 275(2) of the SFA, or to any person pursuant to an offer that is made on terms that such shares, debentures and units of shares and debentures of that corporation or such rights and interest in that trust are acquired at a consideration of not less than $200,000 (or its equivalent in a foreign currency) for each transaction, whether such amount is to be paid for in cash or by exchange of securities or other assets, and further for corporations, in accordance with the conditions, specified in Section 275 of the SFA;

- where no consideration is given for the transfer; or

- where the transfer is by operation of law.

Switzerland

The securities may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange ("SIX") or on any other stock exchange or regulated trading facility in Switzerland. This prospectus supplement has been prepared without regard to the disclosure standards for issuance prospectuses under art. 652a or art. 1156 of the Swiss Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing Rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland. Neither this prospectus supplement nor any other offering or marketing material relating to the securities or the offering may be publicly distributed or otherwise made publicly available in Switzerland.

Neither this prospectus supplement nor any other offering or marketing material relating to the offering, the Company or the securities have been or will be filed with or approved by any Swiss regulatory authority. In particular, this prospectus will not be filed with, and the offer of securities will not be supervised by, the Swiss Financial Market Supervisory Authority FINMA ("FINMA"), and the offer of securities has not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes ("CISA"). The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of securities.

United Kingdom

This prospectus supplement only being distributed to, and is only directed at, persons in the United Kingdom that are qualified investors within the meaning of Article 2(1)(e) of the Prospectus Directive that are also (i) investment professionals falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, as amended (the "Order") and/or (ii) high net worth entities falling within Article 49(2)(a) to (d) of the Order and other persons to whom it may lawfully be communicated (each such person being referred to as a "relevant person").

This prospectus supplement and its contents are confidential and should not be distributed, published or reproduced (in whole or in part) or disclosed by recipients to any other persons in the United Kingdom. Any person in the United Kingdom that is not a relevant person should not act or rely on this document or any of its contents.

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LEGAL MATTERS

K&L Gates LLP, Charlotte, North Carolina, will pass upon certain legal matters relating to this offering. Covington & Burling LLP, New York, New York, is counsel to the underwriters in connection with this offering.

EXPERTS

The consolidated financial statements as of December 31, 2014 and 2013 and for each of the three years in the period ended December 31, 2014 and management's assessment of the effectiveness of internal control over financial reporting as of December 31, 2014 incorporated by reference in this prospectus supplement have been so incorporated in reliance on the reports of BDO USA, LLP, an independent registered public accounting firm, incorporated herein by reference, given on the authority of said firm as experts in auditing and accounting.

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 website maintained by the SEC located at 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, 2014, filed with the SEC on February 27, 2015;
- Our Quarterly Report on Form 10-Q for the quarter ended March 31, 2015 filed with the SEC on May 4, 2015;
- The information contained in the following sections of the proxy statement for our 2015 Annual Meeting filed with the SEC on April 30, 2015: "Information Concerning Directors and Nominees for Director," "Information Concerning Executive Officers," "Section 16(a) Beneficial Ownership Reporting Compliance," "Corporate Governance Principles and Board Matters," "The Board of Directors and Its Committees," "Compensation and Other Information Concerning Directors and Officers," "Report of the Compensation Committee," "Equity Compensation Plan Information," "Securities Ownership of Certain Beneficial Owners and Management," "Certain Relationships and Related Transactions," "Independent Registered Public Accounting Firm" and "Pre-Approval Policies and Procedures;"
- Our Current Reports on Form 8-K filed on February 6, 2015 and February 10, 2015;

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- The description of our common stock contained in our Registration Statement on Form S-1, filed with the SEC on January 30, 2001, including any amendment or reports filed for the purpose of updating such description (Registration No. 333-48812);

- The description of our preferred stock purchase rights contained in our Registration Statement on Form 8-A filed with the SEC on February 23, 2011; 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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EXACT SCIENCES CORPORATION

Common Stock
Preferred Stock
Debt Securities
Warrants

This prospectus relates to common stock, preferred stock, debt securities and warrants that Exact Sciences Corporation may sell from time to time in one or more offerings on terms to be determined at the time of sale. We will provide specific terms of these securities in supplements to this prospectus. You should read this prospectus and any supplement carefully before you invest. This prospectus may not be used to offer and sell securities unless accompanied by a prospectus supplement for those securities.

Our common stock trades on the NASDAQ Capital 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 RISKS. YOU SHOULD REVIEW CAREFULLY THE RISKS AND UNCERTAINTIES DESCRIBED UNDER THE HEADING "RISK FACTORS" CONTAINED IN THE APPLICABLE PROSPECTUS SUPPLEMENT AND ANY RELATED FREE WRITING PROSPECTUS, AND UNDER SIMILAR HEADINGS IN OTHER DOCUMENTS THAT ARE INCORPORATED BY REFERENCE INTO THIS PROSPECTUS OR ANY SUCH PROSPECTUS SUPPLEMENT. SEE "RISK FACTORS" ON PAGE 3 OF THIS PROSPECTUS.

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

The date of this prospectus is July 20, 2015.

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement on Form S-3 that we filed with the SEC utilizing a "shelf" registration process. Under this shelf process, we may from time to time sell any combination of 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 sell securities, we will provide a prospectus supplement that will contain specific information about the terms of the securities being offered. That prospectus supplement may include a discussion of any risk factors or other special consideration that apply to those securities. The prospectus supplement may also add, update or change information contained in this prospectus. If there is any inconsistency between the information in this prospectus and a prospectus supplement, you should rely on the information in that prospectus supplement. You should read both this prospectus and any applicable prospectus supplement together with additional information described above under the heading "Where You Can Find More Information."

When acquiring any securities discussed in this prospectus, you should rely on the information provided in this prospectus and the prospectus supplement, including the information incorporated by reference. Neither we, nor any underwriters or agents, have authorized anyone to provide you with different information. We are not offering the securities in any state where such an offer is prohibited. You should not assume that the information in this prospectus, any prospectus supplement, or any document incorporated by reference, is truthful or complete at any date other than the date mentioned on the cover page of those documents. You should also carefully review the section entitled "Risk Factors", which highlights certain risks associated with an investment in our securities, to determine whether an investment in our securities is appropriate for you.

References in this prospectus to "Exact", the "Company", "we", "us" and "our" are to Exact Sciences Corporation and its subsidiaries.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and special reports, proxy statements and other information with the Securities and Exchange Commission (the "SEC"). You can inspect and copy these reports, proxy statements and other information at the SEC's Public Reference Room at 100 F Street, N.E., Washington, D. C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the Public Reference Room. The SEC also maintains a web site that contains reports, proxy and information statements and other information regarding issuers, such as Exact Sciences Corporation (www.sec.gov). Our web site is located at www.exactsciences.com. The information contained on our web site is not part of this prospectus.

This prospectus "incorporates by reference" certain information that we have filed with the SEC under the Securities Exchange Act of 1934, as amended (the "Exchange Act"). This means we are disclosing important information to you by referring you to those documents. We incorporate by reference the documents listed below and any future filings made by us with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act until the offering is terminated:

Annual Report on Form 10-K for the fiscal year ended December 31, 2014 filed with the SEC on February 27, 2015;

Quarterly Report on Form 10-Q for the quarter ended March 31, 2015 filed with the SEC on May 4, 2015;

The information contained in the following sections of the proxy statement for our 2015 Annual Meeting filed with the SEC on April 30, 2015: "Information Concerning Directors and Nominees for Director," "Information Concerning Executive Officers," "Section 16(a) Beneficial

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Ownership Reporting Compliance," "Corporate Governance Principles and Board Matters," "The Board of Directors and Its Committees," "Compensation and Other Information Concerning Directors and Officers," "Report of the Compensation Committee," "Equity Compensation Plan Information," "Securities Ownership of Certain Beneficial Owners and Management," "Certain Relationships and Related Transactions," "Independent Registered Public Accounting Firm" and "Pre-Approval Policies and Procedures;"

Current Reports on Form 8-K as filed on February 6, 2015 and February 10, 2015;

The description of the Company's Common Stock contained in the Company's Registration Statement on Form S-1, filed with the SEC on January 30, 2001, including any amendment or reports filed for the purpose of updating such description (Registration No. 333-48812); and

The description of the Company's preferred stock purchase rights contained in the Company's Registration Statement on Form 8-A filed with the SEC on February 23, 2011.

You should rely only on the information incorporated by reference or provided in this prospectus. We have authorized no one to provide you with different information. You should not assume that the information in this prospectus is accurate as of any date other than the date on the front of this document. All documents that we file pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act after the date of this prospectus or after the date of the registration statement of which this prospectus forms a part and prior to the termination of the offering will be deemed to be incorporated in this prospectus by reference and will be a part of this prospectus from the date of the filing of the document. Any statement contained in a document incorporated or deemed to be incorporated by reference in this prospectus will be deemed to be modified or superseded for purposes of this prospectus to the extent that a statement contained in this prospectus or in any other subsequently filed document which also is or is deemed to be incorporated by reference in this prospectus modifies or supersedes that statement. Any statement that is modified or superseded will not constitute a part of this prospectus, except as modified or superseded.

We will provide, upon written or oral request, without charge to you, including any beneficial owner to whom this prospectus is delivered, a copy of any or all of the documents incorporated herein by reference other than the exhibits to those documents, unless the exhibits are specifically incorporated by reference into the information that this prospectus incorporates. You should direct a request for copies to us at Attention: Secretary, 441 Charmany Drive, Madison, WI 53719 or you may call us at 608.284.5700.

FORWARD-LOOKING STATEMENTS

Certain information set forth in this prospectus or incorporated by reference in this prospectus 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 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 described in the documents incorporated by reference into this 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

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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.

THE COMPANY

We are a molecular diagnostics company currently focused on the early detection and prevention of some of the deadliest forms of cancer. We have developed an accurate, non-invasive, patient-friendly screening test for the early detection of colorectal pre-cancer and cancer, and we are currently working on the development of tests for lung cancer, pancreatic cancer and esophageal cancer.

Our Cologuard test is designed to detect pre-cancerous lesions or polyps and each of the four stages of colorectal cancer. Cologuard is a non-invasive, stool-based DNA (sDNA) screening test designed to detect DNA markers, which in published studies have been shown to be associated with colorectal cancer. In addition to DNA markers, our test includes a protein marker to detect blood in the stool, utilizing an antibody-based fecal immunochemical test (FIT).

USE OF PROCEEDS

We currently intend to use the estimated net proceeds from the sale of these securities for general corporate and working capital purposes, including to fund our Cologuard commercialization activities and to fund our product development efforts. Accordingly, our management will have significant discretion and flexibility in applying the net proceeds from the sale of these 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.

RATIO OF EARNINGS TO FIXED CHARGES

Our earnings are inadequate to cover fixed charges. The following table sets forth the dollar amount of the coverage deficiency (in thousands) for the periods indicated.

	2015 Q1	2014	2013	2012	2011	2010
Ratio of Earnings to Fixed Charges	*	*	*	*	*	*
Deficiency of Earnings to Cover Fixed Charges	(35,801)	(100,048)	(46,514)	(52,421)	(28,675)	(11,556)

*

During each of these periods, our earnings were less than our fixed charges. The amount of the deficiency for each period is set forth in the above table under the caption "Deficiency of Earnings to Cover Fixed Charges."

RISK FACTORS

Investing in our securities involves risk. See the risk factors described in our Annual Report on Form 10-K for our most recent fiscal year (together with any material changes thereto contained in subsequent filed Quarterly Reports on Form 10-Q) and those contained in our other filings with the SEC, which are incorporated by reference in this prospectus and any accompanying prospectus supplement.

The prospectus supplement applicable to each type or series of securities we offer may contain a discussion of risks applicable to the particular types of securities that we are offering under that prospectus supplement. Prior to making a decision about investing in our securities, you should carefully consider the specific factors discussed under the caption "Risk Factors" in the applicable prospectus supplement, together with all of the other information contained in the prospectus

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supplement or appearing or incorporated by reference in this prospectus. These risks could materially affect our business, results of operations or financial condition and cause the value of our securities to decline. You could lose all or part of your investment.

DESCRIPTION OF SECURITIES WE MAY OFFER

We may issue from time to time, in one or more offerings, the following securities:

- shares of common stock;
- shares of preferred stock;
- debt securities, which may include senior debt securities, subordinated debt securities and senior subordinated debt securities; and
- warrants for the purchase of debt securities, preferred stock or common stock.

Set forth below is a description of the common stock and preferred stock that may be offered under this prospectus. We will set forth in the applicable prospectus supplement and/or free writing prospectus a description of the debt securities and warrants that may be offered under this prospectus. The terms of the offering of our common stock, preferred stock or any such other securities, the initial offering price and the net proceeds to us will be contained in the prospectus supplement, and other offering material, relating to such offer.

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 any such underwriters, dealers or agents, 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 reallowed or paid to dealers and any securities exchanges on which such securities may be listed.

DESCRIPTION OF COMMON STOCK WE MAY OFFER

The following summary description of our common stock is based on the provisions of our certificate of incorporation and bylaws and the applicable provisions of the General Corporation Law of the State of Delaware. This information may not be complete in all respects and is qualified entirely by reference to the provisions of our certificate of incorporation, bylaws and the General Corporation Law of the State of Delaware. For information on how to obtain copies of our certificate of incorporation and bylaws, see the discussion above under the heading "Where You Can Find More Information."

We may offer our common stock issuable upon the conversion of debt securities or preferred stock and upon the exercise of warrants.

Authorized Capital

We currently have authority to issue 200,000,000 shares of our common stock, par value $0.01 per share. As of March 31, 2015, 88,913,304 shares of our common stock were issued and outstanding.

Voting Rights

Each outstanding share of our common stock is entitled to one vote on all matters submitted to a vote of shareholders. There is no cumulative voting.

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Dividend and Liquidation Rights

The holders of outstanding shares of our common stock are entitled to receive dividends out of assets legally available for the payment of dividends at the times and in the amounts as our board of directors may from time to time determine. The shares of our common stock are neither redeemable nor convertible. Holders of our common stock have no preemptive or subscription rights to purchase any securities of Exact. Upon the liquidation, dissolution or winding up of Exact, the holders of our common stock are entitled to receive pro rata the assets of Exact which are legally available for distribution, after payment of all debts and other liabilities and subject to the prior rights of any holders of preferred stock then outstanding.

We have never paid any cash dividends on our common stock.

DESCRIPTION OF PREFERRED STOCK WE MAY OFFER

This section describes the general terms and provisions of the preferred stock we may offer. This information may not be complete in all respects and is qualified entirely by reference to our certificate of incorporation, with respect to each series of preferred stock. The specific terms of any series will be described in a prospectus supplement. Those terms may differ from the terms discussed below. Any series of preferred stock we issue will be governed by our certificate of incorporation and by the certificate of designations relating to that series. We will file the certificate of designations with the SEC and incorporate it by reference as an exhibit to our registration statement at or before the time we issue any preferred stock of that series.

Authorized Preferred Stock

Our certificate of incorporation authorizes us to issue 5,000,000 shares of undesignated preferred stock, par value $0.01 per share. We may issue preferred stock from time to time in one or more series, without shareholder approval, when authorized by our board of directors.

Upon issuance of a particular series of preferred stock, our board of directors is authorized, to specify:

the number of shares to be included in the series;

the annual dividend rate for the series, if any, and any restrictions or conditions on the payment of dividends;

the redemption price, if any, and the terms and conditions of redemption;

any sinking fund provisions for the purchase or redemption of the series;

if the series is convertible, the terms and conditions of conversion;

the amounts payable to holders upon our liquidation, dissolution or winding up; and

any other rights, preferences and limitations relating to the series, including voting rights.

Our board of director's ability to authorize, without shareholder approval, the issuance of preferred stock with conversion and other rights, may adversely affect the rights of holders of our common stock or other series of preferred stock that may be outstanding.

No shares of our preferred stock are currently issued and outstanding.

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Specific Terms of a Series of Preferred Stock

The preferred stock we may offer will be issued in one or more series. The preferred stock will have the dividend, liquidation, redemption and voting rights discussed below, unless otherwise described in a prospectus supplement relating to a particular series. A prospectus supplement will discuss the following features of the series of preferred stock to which it relates:

- the designations and stated value per share;
- the number of shares offered;
- the amount of liquidation preference per share;
- the public offering price at which the preferred stock will be issued;
- the dividend rate, the method of its calculation, the dates on which dividends would be paid and the dates, if any, from which dividends would cumulate;
- any redemption or sinking fund provisions;
- any conversion or exchange rights; and
- any additional voting, dividend, liquidation, redemption, sinking fund and other rights, preferences, privileges, limitations and restrictions.

Rank

Unless otherwise stated in the prospectus supplement, the preferred stock will have priority over our common stock with respect to dividends and distribution of assets, but will rank junior to all our outstanding indebtedness for borrowed money. Any series of preferred stock could rank senior, equal or junior to our other capital stock, as may be specified in a prospectus supplement, as long as our certificate of incorporation so permits.

Dividends

Holders of each series of preferred stock shall be entitled to receive cash dividends to the extent specified in the prospectus supplement when, as and if declared by our board of directors, from funds legally available for the payment of dividends. The rates and dates of payment of dividends of each series of preferred stock will be stated in the prospectus supplement. Dividends will be payable to the holders of record of preferred stock as they appear on our books on the record dates fixed by our board of directors. Dividends on any series of preferred stock may be cumulative or non-cumulative, as discussed in the applicable prospectus supplement.

Convertibility

Shares of a series of preferred stock may be exchangeable or convertible into shares of our common stock, another series of preferred stock or other securities or property. The conversion or exchange may be mandatory or optional. The prospectus supplement will specify whether the preferred stock being offered has any conversion or exchange features, and will describe all the related terms and conditions.

Redemption

The terms, if any, on which shares of preferred stock of a series may be redeemed will be discussed in the applicable prospectus supplement.

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Liquidation

Upon any voluntary or involuntary liquidation, dissolution or winding up of the affairs of Exact, holders of each series of preferred stock will be entitled to receive distributions upon liquidation in the amount described in the related prospectus supplement. These distributions will be made before any distribution is made on any securities ranking junior to the preferred stock with respect to liquidation, including our common stock. If the liquidation amounts payable relating to the preferred stock of any series and any other securities ranking on a parity regarding liquidation rights are not paid in full, the holders of the preferred stock of that series will share ratably in proportion to the full liquidation preferences of each security. Holders of our preferred stock will not be entitled to any other amounts from us after they have received their full liquidation preference.

Voting

The holders of preferred stock of each series will have no voting rights, except as required by law and as described below or in a prospectus supplement. Our board of directors may, upon issuance of a series of preferred stock, grant voting rights to the holders of that series to elect additional board members if we fail to pay dividends in a timely fashion.

Without the affirmative vote of a majority of the shares of preferred stock of any series then outstanding, we may not:

increase or decrease the aggregate number of authorized shares of that series;

increase or decrease the par value of the shares of that series; or

alter or change the powers, preferences or special rights of the shares of that series so as to affect them adversely.

No Other Rights

The shares of a series of preferred stock will not have any preferences, voting powers or relative, participating, optional or other special rights except:

as discussed above or in the prospectus supplement;

as provided in our certificate of incorporation and in the certificate of designations; and

as otherwise required by law.

PLAN OF DISTRIBUTION

We may sell the securities offered by this prospectus to one or more underwriters or dealers for public offering, through agents, directly to purchasers or through a combination of any such methods of sale. The name of any such underwriters, dealers or agents involved in the offer and sale of the securities, the amounts underwritten and the nature of its obligation to take the securities will be specified in the applicable prospectus supplement. We have reserved the right to sell the securities directly to investors on our own behalf in those jurisdictions where we are authorized to do so. The sale of the securities may be effected in transactions (a) on any national or international securities exchange or quotation service on which the securities may be listed or quoted at the time of sale, (b) in the over-the-counter market, (c) in transactions otherwise than on such exchanges or in the over-the-counter market or (d) through the writing of options.

We and our agents and underwriters may offer and sell the securities at a fixed price or prices that may be changed, at market prices prevailing at the time of sale, at prices related to such prevailing market prices or at negotiated prices. The securities may be offered on an exchange, which will be disclosed in the applicable prospectus supplement. We may, from time to time, authorize dealers, acting

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as our agents, to offer and sell the securities upon such terms and conditions as set forth in the applicable prospectus supplement.

If we use underwriters to sell securities, we will enter into an underwriting agreement with them at the time of the sale to them. In connection with the sale of the securities, underwriters may receive compensation from us in the form of underwriting discounts or commissions and may also receive commissions from purchasers of the securities for whom they may act as agent. Any underwriting compensation paid by us to underwriters or agents in connection with the offering of the securities, and any discounts, concessions or commissions allowed by underwriters to participating dealers, will be set forth in the applicable prospectus supplement to the extent required by applicable law. Underwriters may sell the securities to or through dealers, and such dealers may receive compensation in the form of discounts, concessions or commissions from the underwriters or commissions (which may be changed from time to time) from the purchasers for whom they may act as agents.

Dealers and agents participating in the distribution of the securities may be deemed to be underwriters, and any discounts and commissions received by them and any profit realized by them on resale of the securities may be deemed to be underwriting discounts and commissions under the Securities Act. Unless otherwise indicated in the applicable prospectus supplement, an agent will be acting on a best efforts basis and a dealer will purchase debt securities as a principal, and may then resell the debt securities at varying prices to be determined by the dealer.

If so indicated in the prospectus supplement, we will authorize underwriters, dealers or agents to solicit offers by certain specified institutions to purchase offered securities from us at the public offering price set forth in the prospectus supplement pursuant to delayed delivery contracts providing for payment and delivery on a specified date in the future. Such contracts will be subject to any conditions set forth in the applicable prospectus supplement and the prospectus supplement will set forth the commission payable for solicitation of such contracts. The underwriters and other persons soliciting such contracts will have no responsibility for the validity or performance of any such contracts.

Underwriters, dealers and agents may be entitled, under agreements entered into with us, to indemnification against and contribution towards certain civil liabilities, including any liabilities under the Securities Act.

To facilitate the offering of securities, certain persons participating in the offering may engage in transactions that stabilize, maintain, or otherwise affect the price of the securities. These may include over-allotment, stabilization, syndicate short covering transactions and penalty bids. Over-allotment involves sales in excess of the offering size, which creates a short position. Stabilizing transactions involve bids to purchase the underlying security so long as the stabilizing bids do not exceed a specified maximum. Syndicate short covering transactions involve purchases of securities in the open market after the distribution has been completed in order to cover syndicate short positions. Penalty bids permit the underwriters to reclaim selling concessions from dealers when the securities originally sold by the dealers are purchased in covering transactions to cover syndicate short positions. These transactions may cause the price of the securities sold in an offering to be higher than it would otherwise be. These transactions, if commenced, may be discontinued by the underwriters at any time.

Any securities other than our common stock issued hereunder may be new issues of securities with no established trading market. Any underwriters or agents to or through whom such securities are sold for public offering and sale may make a market in such securities, but such underwriters or agents will not be obligated to do so and may discontinue any market making at any time without notice. No assurance can be given as to the liquidity of the trading market for any such securities. The amount of expenses expected to be incurred by us in connection with any issuance of securities will be set forth in the applicable prospectus supplement. Certain of the underwriters, dealers or agents and their

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associates may engage in transactions with, and perform services for, us and certain of our affiliates in the ordinary course of business.

During such time as we may be engaged in a distribution of the securities covered by this prospectus we are required to comply with Regulation M promulgated under the Exchange Act. With certain exceptions, Regulation M precludes us, any affiliated purchasers, and any broker-dealer or other person who participates in such distribution from bidding for or purchasing, or attempting to induce any person to bid for or purchase, any security which is the subject of the distribution until the entire distribution is complete. Regulation M also restricts bids or purchases made in order to stabilize the price of a security in connection with the distribution of that security. All of the foregoing may affect the marketability of our shares of common stock.

LEGAL MATTERS

The validity and legality of the securities offered hereby and certain other legal matters will be passed upon for the Company by K&L Gates LLP, Charlotte, North Carolina 28202.

EXPERTS

The financial statements as of December 31, 2014 and 2013 and for each of the three years in the period ended December 31, 2014 and management's assessment of the effectiveness of internal control over financial reporting as of December 31, 2014 incorporated by reference in this prospectus have been so incorporated in reliance on the reports of BDO USA, LLP, an independent registered public accounting firm, incorporated herein by reference, given on the authority of said firm as experts in auditing and accounting.

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7,000,000 Shares

Exact Sciences Corporation

Common Stock

PROSPECTUS SUPPLEMENT

Joint Book-Running Managers

Jefferies

Baird

July 21, 2015