

EXACT SCIENCES CORP
Form 424B5
June 06, 2017

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Filed Pursuant to Rule 424(b)(5)
Registration No. 333-218535

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

SUBJECT TO COMPLETION, DATED JUNE 6, 2017

**PROSPECTUS SUPPLEMENT
(To Prospectus dated June 6, 2017)**

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 June 5, 2017, the last reported sale price of our common stock on the NASDAQ Capital Market was \$37.07 per share.

The underwriters have agreed to purchase the common stock from us at a price of \$ per share, which will result in \$ of proceeds to us (before expenses). The underwriters may offer the common shares from time to time for sale in one or more transactions on the NASDAQ Capital Market, in the over-the-counter market, through negotiated transactions or otherwise at market prices prevailing at the time of sale, at prices related to prevailing market prices or at negotiated prices. The underwriters will be reimbursed for certain expenses incurred in this offering. See "Underwriting" for details.

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.

Investing in our common stock involves a high degree of risk. Please read "Risk Factors" beginning on page S-9 of this prospectus supplement, on page S-1 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.

The underwriters expect to deliver the shares of common stock on or about June , 2017.

Joint Book-Running Managers

Jefferies

BofA Merrill Lynch

Baird

Prospectus Supplement dated June , 2017.

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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 together with all documents incorporated by reference.

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 and in any free writing prospectuses we may provide to you in connection with this offering. 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. The information in this prospectus supplement, the accompanying prospectus and in any free writing prospectuses we may provide to you in connection with this offering is accurate only as of their respective dates, regardless of time of delivery. Our business, financial condition, results of operations and prospects may have changed since those dates. Our business, financial condition, results of operations and prospects may have changed since those dates.

We are offering to sell, and seeking offers to buy, our securities only in jurisdictions where offers and sales are permitted. The distribution of this prospectus supplement and the offering of the securities in certain jurisdictions may be restricted by law. Persons outside the United States who come into possession of this prospectus supplement must inform themselves about, and observe any restrictions relating to, the offering of the securities and the distribution of this prospectus supplement outside the United States. This prospectus supplement does not constitute, and may not be used in connection with, an offer to sell, or a solicitation of an offer to buy, any securities offered by this prospectus supplement by any person in any jurisdiction in which it is unlawful for such person to make such an offer or solicitation.

All references in this prospectus 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. All statements other than statements of historical facts included in this prospectus supplement regarding our strategies, prospects, financial condition, operations, costs, plans and objectives are forward-looking statements. Examples of forward-looking statements include, among others, statements we make regarding expected future operating results, anticipated results of our sales and marketing efforts, expectations concerning payor reimbursement and the anticipated results of our product development efforts. Forward-looking statements are neither historical facts nor assurances of future performance. Instead, they are based only on our current beliefs, expectations and assumptions regarding the future of our business, future plans and strategies, projections, anticipated events and trends, the economy and other future conditions. Because forward-looking statements relate to the future, they are subject to inherent uncertainties, risks and changes in circumstances that are difficult to predict and many of which are outside of our control. Our actual results and financial condition may differ materially from those in the forward-looking statements. Therefore, you should not rely on any of these forward-looking statements. Important factors that could cause our actual results and financial condition to differ materially from those indicated in the forward-looking statements include, among others, the following: our ability to successfully and profitably market our products and services; the acceptance of our products and services by patients and healthcare providers; our ability to meet demand for our products and services; the willingness of health insurance companies and other payors to cover Cologuard and reimburse us for our performance of the Cologuard test; the amount and nature of competition from other cancer screening products and services; the effects of the adoption, modification or repeal of any healthcare reform law, rule, order, interpretation or policy; the effects of changes in healthcare pricing, coverage and reimbursement; recommendations, guidelines and quality metrics issued by various organizations such as the U.S. Preventive Services Task Force, the American Cancer Society, and the National Committee for Quality Assurance regarding cancer screening or our products and services; our ability to successfully develop new products and services; our success establishing and maintaining collaborative, licensing and supplier arrangements; our ability to maintain regulatory approvals and comply with applicable regulations; and the other 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. Therefore, you should not rely on any of these forward-looking statements. 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 undertake no obligation to publicly update any forward-looking statement, whether written or oral, that may be made from time to time, whether as a result of new information, future developments or otherwise.

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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 called Cologuard for the early detection of colorectal cancer and pre-cancer, and we are currently working on the development of additional tests for other types of cancer, with the goal of becoming a leader in cancer diagnostics.

Our Cologuard® Test

Colorectal cancer is the second leading cause of cancer deaths in the United States and the leading cause of cancer deaths in the U.S. among non-smokers. Each year in the U.S. there are approximately:

135,000 new cases of colorectal cancer

50,000 deaths from colorectal cancer

Colorectal cancer treatment represents a significant, growing healthcare cost. As of 2010, \$14 billion was spent annually in the U.S. on colorectal cancer treatment, and the projected annual treatment costs are expected to be \$20 billion in 2020. The incidence of colorectal cancer in Medicare patients is expected to rise from 106,000 cases in 2010 to more than 180,000 cases in 2030.

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 U.S. for whom routine colorectal cancer screening is recommended, 38 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 underserved population of unscreened and inadequately screened patients represents a significant opportunity for a patient-friendly screening test.

Our Cologuard test is a non-invasive stool-based DNA (sDNA) screening test which utilizes a multi-target approach to detect DNA and hemoglobin biomarkers associated with colorectal cancer and pre-cancer. Eleven biomarkers are targeted that have been shown to be strongly associated with colorectal cancer and pre-cancer. Methylation, mutation, and hemoglobin results are combined in the laboratory analysis through a proprietary algorithm to provide a single positive or negative reportable result.

On August 11, 2014, the U.S. Food and Drug Administration (FDA) approved Cologuard for use as the first and only sDNA non-invasive colorectal cancer screening test. Our submission to the FDA for Cologuard included the results of our pivotal DeeP-C clinical trial that had over 10,000 patients

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enrolled at 90 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%

Stage I and II Cancer Sensitivity: 94%

High-Grade Dysplasia Sensitivity: 69%

Specificity: 87%

The competitive advantages of sDNA screening may provide a significant market opportunity. If the test were used by 30 percent of the eligible screening population at a three-year screening interval rate, we estimate the potential U.S. market for sDNA screening would be more than \$4 billion, annually.

Our commercialization strategy includes three main elements focusing on physicians, patients, and payors.

Our sales team actively engages with physicians and their staffs to emphasize the need for colorectal cancer screening, educate them on the value of Cologuard, and enroll them in our physician ordering system to enable them to prescribe the test. We focus on specific physicians based on Cologuard order history and on physician groups and larger regional and national health systems.

Securing inclusion in guidelines and quality measures is a key part of our physician engagement strategy since many physicians rely on such guidelines and quality measures when making screening recommendations. In June 2016, the US Preventive Services Task Force (USPSTF) issued an updated recommendation statement for colorectal cancer screening and gave an "A" grade to colorectal cancer screening starting at age 50 and continuing until age 75. The statement specifies seven screening methods, including FIT-DNA (which is Cologuard).

In October 2016, the National Committee for Quality Assurance (NCQA) included Cologuard testing on a three-year interval in the 2017 Healthcare Effectiveness Data and Information Set (HEDIS) measures. More than 90 percent of America's health plans measure quality based on HEDIS. In April 2017, the Centers for Medicare & Medicaid Services ("CMS") included Cologuard in its updated 2018 Medicare Advantage Star Ratings program. Medicare Advantage plans are eligible to receive quality credit under the Star Ratings program for Cologuard tests completed in 2014, 2015, 2016 and beyond.

A critical part of the value proposition of Cologuard is our compliance program, which involves active engagement with patients and physicians. This customer-service-oriented activity is focused on helping patients to complete Cologuard tests that have been ordered for them by their physicians and supporting physicians in their efforts to have their patients screened.

After the launch of Cologuard, we initiated a significant public relations effort to engage patients in the United States. We have conducted targeted direct-to-patient advertising campaigns through social media, print and other channels. In 2016 we began a national television advertising campaign. To date, we have focused our efforts on cable television most commonly viewed by our target patient demographic. In 2017, we plan to continue our targeted direct-to-patient advertising initiatives and launch new content for our television advertising campaign.

The cornerstone of our payor-engagement strategy was securing coverage from CMS. Medicare covers 47% of patients in the screening population for Cologuard. On October 9, 2014, CMS issued a National Coverage Determination (NCD) for Cologuard following a parallel review process with FDA. Cologuard was the first screening test approved by FDA and covered by CMS through that process. As

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outlined in the NCD, Medicare Part B covers 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 for developing colorectal cancer (e.g., 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 non-polyposis colorectal cancer).

In the 2017 Clinical Laboratory Fee Schedule (CLFS), CMS established reimbursement for Cologuard at \$512.43. Payments from CMS are subject to sequestration. Under the Protecting Access to Medicare Act of 2014 (PAMA), we anticipate that effective January 1, 2018, the CMS reimbursement rate for Cologuard will be calculated based on the volume-weighted median of private payor rates for Cologuard. The initial data collection period for that purpose was the period between January 1, 2016 and June 30, 2016. The CMS reimbursement rate will subsequently be reset every three years, or every year if the Company applies for, and is granted, Advanced Diagnostic Laboratory Test status for Cologuard, based on the volume-weighted median of private payor rates experienced in the applicable six-month data collection period. We submitted data for the initial collection period in March 2017, and our data submission will be subject to review by CMS prior to the finalization of the new reimbursement rate for Cologuard.

In addition to Medicare reimbursement, we believe it is necessary to secure favorable coverage and in-network reimbursement agreements from commercial payors for Cologuard to achieve its full commercial potential. Some commercial payors have issued positive coverage decisions for Cologuard and others have agreed to cover Cologuard as an in-network service. We believe that commercial payors' reimbursement of Cologuard will depend on a number of factors, including payors' determination that it is: sensitive and specific for colorectal cancer; not experimental or investigational; approved or recommended by major organizations' guidelines; subject to applicable federal and state coverage mandates; reliable, safe and effective; medically necessary; appropriate for the specific patient; and cost-effective. Also, some payors may require that they give prior authorization for a Cologuard test before they are willing to pay for it. Prior authorization requirements may include requirements that we, patients, or physicians provide the payor with extensive medical records and other information.

Coverage of Cologuard may also depend, in whole or in part, on whether payors determine, or courts and/or regulatory authorities determine, coverage is required under applicable federal or state laws mandating coverage of certain colorectal cancer screening services. For example, Section 2713 of the Patient Protection and Affordable Care Act (ACA) mandates that certain health insurers cover evidence-based items or services that have in effect a rating of "A" or "B" in the current recommendations of USPSTF without imposing any patient cost-sharing (ACA Mandate). Similarly, federal regulations require that Medicare Advantage plans cover "A" or "B" rated preventive services without patient cost-sharing. Following the June 2016 update to the USPSTF colorectal cancer screening recommendation statement, CMS issued an updated Evidence of Coverage notice for Medicare Advantage plans that affirms such plans must include coverage of Cologuard every three years without patient cost-sharing. While we believe the ACA Mandate will require certain health insurers to cover Cologuard without patient cost-sharing (following an initial phase-in period between one and two years from the date of the updated USPSTF recommendation statement), it is possible that certain health insurers will disagree, in which case courts and/or governmental agencies may need to resolve the matter. It is also possible that the ACA Mandate will be repealed or significantly modified in the future.

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Similarly, we believe the laws of approximately 30 states currently mandate coverage of Cologuard by certain health insurance plans. While some insurers have agreed with our interpretation with regard to certain states, other insurers have disagreed with regard to other states. In some cases, we have filed lawsuits in an effort to enforce state laws we believe require coverage of Cologuard, and we may file additional suits in the future. We may or may not be successful in any such lawsuit.

We are pursuing a variety of strategies to increase commercial payor coverage for Cologuard, including providing cost effectiveness data to payors to make the case for Cologuard reimbursement. We are focusing our efforts on large national and regional insurers, insurers in states with coverage mandates for colorectal cancer screening, and health plans that have affiliated health systems.

We believe quality metrics may influence payors' coverage decisions, as well as physicians' cancer screening procedures. Some government and private payors are adopting pay-for-performance programs that differentiate payments for healthcare services based on the achievement of documented quality metrics, cost efficiencies or patient outcomes. Payors may look to quality measures such as the HEDIS and CMS Star Ratings measures to assess quality of care. We believe inclusion in the HEDIS measures and Star Ratings measures may have a positive impact on payors' willingness to reimburse Cologuard, as well as on physicians' willingness to prescribe the test.

As part of our commercialization strategy, we established a state-of-the-art, highly automated lab facility that is certified pursuant to federal Clinical Laboratory Improvement Amendments (CLIA) requirements to process Cologuard tests and provide patient results. Our commercial lab operation is housed in a 50,000 square foot facility in Madison, Wisconsin. At our lab, we currently have the capacity to process approximately one million tests per year. We are currently exploring opportunities to increase our capacity to two million tests per year at our existing lab facility, which includes expanding our current lab facility. We are also evaluating options for a second lab facility to add capacity in excess of two million tests per year.

We also are developing a pipeline of potential future products and services. We are continuing to collaborate with MAYO Foundation for Medical Education and Research (MAYO) on developing new tests, with the goal of becoming a leader in cancer diagnostics. We believe Cologuard's technological platform provides a strong foundation for the development of additional cancer diagnostic tests. Through our collaboration with MAYO, we have identified proprietary methylation markers for several major cancers. We have successfully performed validation studies on tissue samples for seven major cancers, including lung cancer, and on blood samples for four major cancers.

The ACS estimates that lung cancer will be diagnosed in 223,000 Americans and cause 156,000 deaths in the United States in 2017. 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. We are currently developing a blood-based biomarker test to aid in the early detection of lung cancer in individuals with lung nodules discovered through a computerized tomography (CT) or other scan. Such a test may help reduce the number of unnecessary biopsies and other follow-up procedures, and thereby reduce costs and improve health outcomes. We recently completed a multi-round study of nearly 400 patients, which demonstrated high accuracy for detecting lung cancer at all stages.

We also continue to explore opportunities for improving Cologuard, including improvements that could lower our cost of sales.

Our top priorities for 2017 are to (1) grow revenue for Cologuard, which includes leveraging Cologuard's growth towards becoming a standard of care, (2) improve the customer experience and continue to deliver world class service to patients and providers, and (3) expand our product portfolio by developing additional cancer diagnostic tests.

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Corporate Information

Our executive offices are located at 441 Charmany Drive, Madison, Wisconsin 53719. Our telephone number is (608) 284-5700. Our Internet website address is 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: | 118,197,740 shares (or 119,247,740 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 including to increase our laboratory, manufacturing and customer service capacity, 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-9 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 111,197,740 shares outstanding as of March 31, 2017, and includes 92,376 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, 2017:

3,613,395 shares subject to outstanding stock options at a weighted average exercise price of \$7.50 per share;

5,460,747 shares subject to outstanding restricted stock unit awards; or

3,047,910 additional shares of common stock reserved for issuance under our equity incentive plans (or 12,700,000 additional shares, subject to stockholder approval of an amendment to our 2010 Omnibus Long-Term Incentive Plan (As Amended and Restated Effective April 28, 2015) at our 2017 annual stockholder meeting scheduled for July 27, 2017).

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 119,247,740 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

An investment in our common stock involves a high degree of risk. You should carefully consider the risk factors contained in our most recently filed periodic reports filed with the SEC, including our Annual Report on Form 10-K for the fiscal year ended December 31, 2016, which are incorporated by reference into this prospectus supplement. Before making an investment decision, you should carefully consider these risks as well as other information we include or incorporate by reference in this prospectus supplement. Additional risks and uncertainties not presently known to us or that we deem currently immaterial may also impair our business, operating results and financial condition and could result in a complete loss of your investment.

Risks Related to the Offering

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.

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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 \$ _____, 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 \$ _____ 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 including to increase our laboratory, manufacturing and customer service capacity, 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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Our net tangible book value as of March 31, 2017, was \$308.0 million, or \$2.77 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, 2017. After giving effect to our sale of 7,000,000 of shares of common stock in this offering at the public offering price of \$ _____ 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, 2017, would have been \$ _____ million, or \$ _____ per share. This represents an immediate increase in net tangible book value of \$ _____ per share to existing stockholders and an immediate dilution in net tangible book value of \$ _____ per share to purchasers of common stock in this offering. The following table illustrates this calculation.

| | |
|---|---------|
| Public offering price per share of common stock | \$ |
| Net tangible book value per share as of March 31, 2017 | \$ 2.77 |
| Increase per share attributable to this offering | \$ |
| As adjusted net tangible book value per share after this offering | \$ |
| Dilution per share to new investors in this offering | \$ |

If the underwriters exercise their option to purchase additional shares in full, our as adjusted net tangible book value per share at March 31, 2017, after giving effect to this offering, would have been \$ _____ per share, and the dilution to purchasers in this offering would have been \$ _____ per share.

The number of shares outstanding after the offering is based on 111,197,740 shares outstanding as of March 31, 2017, and includes 92,376 shares of unvested restricted stock held by directors. The number of outstanding shares after the offering does not include, in each case as of March 31, 2017:

3,613,395 shares subject to outstanding stock options at a weighted average exercise price of \$7.50 per share;

5,460,747 shares subject to outstanding restricted stock unit awards; or

3,047,910 additional shares of common stock reserved for issuance under our equity incentive plans (or 12,700,000 additional shares, subject to stockholder approval of an amendment to our 2010 Omnibus Long-Term Incentive Plan (As Amended and Restated Effective April 28, 2015) at our 2017 annual stockholder meeting scheduled for July 27, 2017).

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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 (the "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 Internal Revenue Service ("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 for U.S. federal income tax purposes:

a nonresident alien individual;

a foreign corporation; or

an estate or a trust that, in either case, is not subject to U.S. federal income tax on a net income basis on income or gain from the common stock.

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 the U.S. federal alternative minimum tax, 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;

regulated investment companies or real estate investment trusts;

pension plans;

controlled foreign corporations;

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passive foreign investment companies;

persons who received our common stock as compensation;

brokers and dealers in securities or currencies;

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 an income tax treaty, a non-U.S. holder must provide a properly executed IRS Form W-8BEN or W-8BEN-E, as applicable (or successor form to either), certifying under penalties of perjury that such non-U.S. holder is entitled to benefits under the applicable income tax treaty and has complied with any special certification requirements 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. Non-U.S. holders should consult with their own tax advisors regarding possible entitlements to benefits under any income tax treaty.

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.

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

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

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" under Section 897 of the Code.

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.

Information Reporting and Backup Withholding

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, currently imposed at a rate of 28%, 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 or W-8BEN-E, as applicable) 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

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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. Rather, amounts withheld under the backup withholding rules from a payment to a non-U.S. holder can be refunded or credited against the non-U.S. holder's U.S. federal income tax liability, if any, provided that certain required information is furnished to the IRS in a timely manner.

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 or other tax treaty provides otherwise.

Foreign Account Tax Compliance Act

In addition to the withholding described above, legislation enacted in 2010, known as the Foreign Account Tax Compliance Act ("FATCA") imposes a 30% withholding tax on dividend payments made by a U.S. person to a foreign financial institution or non-financial foreign entity (including, in some cases, when a foreign financial institution or nonfinancial foreign entity is acting as an intermediary), and on the gross proceeds received by a foreign financial institution or non-financial foreign entity as a result of a sale or other disposition of shares of stock issued by a U.S. person (on or after January 1, 2019), unless (i) in the case of a foreign financial institution, such institution enters into (or is deemed to have entered into) an agreement with the U.S. Treasury Department to withhold on certain payments, and to collect and provide to the U.S. Treasury Department substantial information regarding U.S. account holders of such institution (which includes certain equity and debt holders of such institution, as well as certain account holders that are foreign entities with U.S. owners), (ii) in the case of a non-financial foreign entity, such entity provides the withholding agent with a certification identifying the direct and indirect substantial U.S. owners of the entity, or (iii) the foreign financial institution or non-financial foreign entity otherwise qualifies for an exemption from these rules.

Non-U.S. Holders should consult with their own tax advisors regarding the possible implications of FATCA to such holders in connection with this transaction.

Table of Contents**UNDERWRITING**

Subject to the terms and conditions set forth in the underwriting agreement, dated June , 2017, between us and Jefferies LLC, Merrill Lynch, Pierce, Fenner & Smith Incorporated and Robert W. Baird & Co. Incorporated, as the joint book-running managers, 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 | |
| Merrill Lynch, Pierce, Fenner & Smith Incorporated | |
| Robert W. Baird & Co. Incorporated | |
| 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 \$ per share, which will result in \$ of proceeds to us before expenses (or approximately \$ if the underwriters' option to purchase additional shares described below is exercised in full). The underwriters may offer the common stock from time to time for sale in one or more transactions on the NASDAQ Capital Market, in the over-the-counter market, through negotiated transactions or otherwise at market prices prevailing at the time of sale, at prices related to prevailing market prices or at negotiated prices. In connection with the sale of the common stock offered hereby, the underwriters may be deemed to have received compensation in the form of an underwriting discount. The underwriters may effect such transactions by selling common stock to or through dealers, and such dealers may receive compensation in the form of discounts, concessions or commissions from the

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underwriters and / or purchasers of common stock for whom they may act as agents or to whom they may sell as principal.

The expenses of this offering, not including the underwriting discount, are estimated at \$700,000 and are payable by us. We have agreed to reimburse the underwriters in an amount of up to \$10,000 for expenses relating to the compliance of this offering with the rules of the Financial Industry Regulatory Authority, Inc. ("FINRA"). In accordance with FINRA Rule 5110, this reimbursed FINRA 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, Merrill Lynch, Pierce, Fenner & Smith Incorporated 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.

Jefferies LLC, Merrill Lynch, Pierce, Fenner & Smith Incorporated 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

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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.

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

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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

Canada

Resale Restrictions

The distribution of the securities in Canada is being made only in the provinces of Ontario, Quebec, Alberta and British Columbia on a private placement basis exempt from the requirement that we prepare and file a prospectus with the securities regulatory authorities in each province where trades of these securities are made. Any resale of the securities in Canada must be made under applicable securities laws which may vary depending on the relevant jurisdiction, and which may require resales to be made under available statutory exemptions or under a discretionary exemption granted by the applicable Canadian securities regulatory authority. Purchasers are advised to seek legal advice prior to any resale of the securities.

Representations of Canadian Purchasers

By purchasing the securities in Canada and accepting delivery of a purchase confirmation, a purchaser is representing to us and the dealer from whom the purchase confirmation is received that:

the purchaser is entitled under applicable provincial securities laws to purchase the securities without the benefit of a prospectus qualified under those securities laws as it is an "accredited investor" as defined under National Instrument 45-106 Prospectus Exemptions,

the purchaser is a "permitted client" as defined in National Instrument 31-103 Registration Requirements, Exemptions and Ongoing Registrant Obligations,

where required by law, the purchaser is purchasing as principal and not as agent, and

the purchaser has reviewed the text above under Resale Restrictions.

Conflicts of Interest

Canadian purchasers are hereby notified that Jefferies LLC, Merrill Lynch, Pierce, Fenner & Smith Incorporated and Robert W. Baird & Co. Incorporated are relying on the exemption set out in section 3A.3 or 3A.4, if applicable, of National Instrument 33-105 Underwriting Conflicts from having to provide certain conflict of interest disclosure in this document.

Statutory Rights of Action

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if the prospectus (including any amendment thereto) such as this document contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser's province or territory. The purchaser of these securities in Canada should refer to any applicable provisions of the securities legislation of the purchaser's province or territory for particulars of these rights or consult with a legal advisor.

Enforcement of Legal Rights

All of our directors and officers as well as the experts named herein may be located outside of Canada and, as a result, it may not be possible for Canadian purchasers to effect service of process within Canada upon us or those persons. All or a substantial portion of our assets and the assets of those persons may be located outside of Canada and, as a result, it may not be possible to satisfy a judgment against us or those persons in Canada or to enforce a judgment obtained in Canadian courts against us or those persons outside of Canada.

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Taxation and Eligibility for Investment

Canadian purchasers of the securities should consult their own legal and tax advisors with respect to the tax consequences of an investment in the securities in their particular circumstances and about the eligibility of the securities for investment by the purchaser under relevant Canadian legislation.

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 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;

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

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.

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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.

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

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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, 2016 and 2015 and for each of the three years in the period ended December 31, 2016 and management's assessment of the effectiveness of internal control over financial reporting as of December 31, 2016 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, 2016, filed with the SEC on February 21, 2017;

Our Quarterly Report on Form 10-Q for the quarter ended March 31, 2017 filed with the SEC on April 27, 2017;

Our Current Report on Form 8-K as filed on April 27, 2017;

The information contained in the following sections of the proxy statement for our 2017 Annual Meeting filed with the SEC on April 28, 2017: "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;"

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The description of the Company's Common Stock contained in the Company's Registration Statement on Form 8-A, filed with the SEC pursuant to Section 12(g) of the Exchange Act on December 26, 2000, including any amendment or reports filed for the purpose of updating such description;

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.

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 4 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 June 6, 2017.

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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 headings "Where You Can Find More Information" and "Incorporation by Reference."

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.

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.

INCORPORATION BY REFERENCE

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

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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, 2016 filed with the SEC on February 21, 2017;

Quarterly Report on Form 10-Q for the quarter ended March 31, 2017 filed with the SEC on April 27, 2017;

Current Report on Form 8-K filed with the SEC on April 27, 2017;

The information contained in the following sections of the proxy statement for our 2016 Annual Meeting filed with the SEC on April 28, 2017: "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;"

The description of the Company's Common Stock contained in the Company's Registration Statement on Form 8-A, filed with the SEC pursuant to Section 12(g) of the Exchange Act on December 26, 2000, including any amendment or reports filed for the purpose of updating such description; 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 pursuant to Section 12(b) of the Exchange Act 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.

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. All statements other than statements of historical facts included in this prospectus regarding our strategies, prospects, financial condition, operations, costs, plans and objectives are

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forward-looking statements. Examples of forward-looking statements include, among others, statements we make regarding expected future operating results, anticipated results of our sales and marketing efforts, expectations concerning payor reimbursement and the anticipated results of our product development efforts. Forward-looking statements are neither historical facts nor assurances of future performance. Instead, they are based only on our current beliefs, expectations and assumptions regarding the future of our business, future plans and strategies, projects, anticipated events and trends, the economy and other future conditions. Because forward-looking statements relate to the future, they are subject to inherent uncertainties, risks and changes in circumstances that are difficult to predict and many of which are outside our control. Our actual results and financial condition may differ materially from those in the forward-looking statements, as a result of various factors, including those risks and uncertainties included in this prospectus under the caption "Risk Factors," and those risks and uncertainties described in the documents incorporated by reference into this prospectus. Therefore, you should not rely on any of these forward-looking statements. 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 undertake no obligation to publicly update any forward-looking statement, whether written or oral, that may be made from time to time, whether as a result of new information, future developments or otherwise.

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 called Cologuard® for the early detection of colorectal cancer and pre-cancer, and we are currently working on the development of additional tests for other types of cancer, with the goal of becoming a leader in cancer diagnostics.

Our Cologuard test is a non-invasive stool-based DNA (sDNA) screening test which utilizes a multi-target approach to detect DNA and hemoglobin biomarkers associated with colorectal cancer and pre-cancer. Eleven biomarkers are targeted that have been shown to be strongly associated with colorectal cancer and pre-cancer. Methylation, mutation, and hemoglobin results are combined in the laboratory analysis through a proprietary algorithm to provide a single positive or negative reportable result.

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 expansion of 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.

Table of Contents**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.

| | 2017 Q1 | 2016 | 2015 | 2014 | 2013 | 2012 |
|---|----------|-----------|-----------|-----------|----------|----------|
| Ratio of Earnings to Fixed Charges | * | * | * | * | * | * |
| Deficiency of Earnings to Cover Fixed Charges | (34,946) | (167,211) | (157,803) | (100,048) | (46,514) | (52,421) |

*

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 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

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

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, 2017, 111,197,740 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.

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.

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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 directors' 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.

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

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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.

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.

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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 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

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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 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, 2016 and 2015 and for each of the three years in the period ended December 31, 2016 and management's assessment of the effectiveness of internal control over financial reporting as of December 31, 2016 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
BofA Merrill Lynch
Baird**

June , 2017
