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Filed Pursuant to Rule 424(b)(7)
Registration No. 333-218535

CALCULATION OF REGISTRATION FEE

Title of Each Class of Securities to be Registered	Amount to be Registered(1)	Proposed Maximum Offering Price per Unit(2)	Proposed Maximum Aggregate Offering Price(2)	Amount of Registration Fee(3)
Common Stock, par value $0.01 per share	533,763	$78.55	$41,924,414.84	$5,441.79

(1) Pursuant to Rule 416(a) under the Securities Act of 1933, as amended (the "Securities Act"), this registration statement also registers such additional shares of common stock as may become issuable to prevent dilution as a result of stock splits, stock dividends or similar transactions.

(2) Estimated solely for the purpose of calculating the registration fee pursuant to Rule 457(c) under the Securities Act. Based on the average of the high and low reported trading prices of common stock as reported on the Nasdaq Capital Market on March 2, 2020.

(3) Calculated in accordance with Rule 457(r) of the Securities Act. This "Calculation of Registration Fee" table shall be deemed to update the "Calculation of Registration Fee" table in the registrant's Registration Statement on Form S-3ASR (File No. 333-218535) in accordance with Rules 456(b) and 457(r) under the Securities Act.

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PROSPECTUS SUPPLEMENT
(To prospectus dated June 6, 2017)

EXACT SCIENCES CORPORATION

533,763 Shares of Common Stock

This prospectus supplement relates to the resale of up to 533,763 shares of our common stock, par value $0.01 per share, from time to time in one or more offerings by selling stockholders named herein and any additional selling stockholders who will be identified in one or more prospectus supplements. We will not receive any proceeds from the resale of any of the shares of our common stock being registered hereby.

The shares offered hereby were issued or are issuable to the selling stockholders in connection with our acquisitions of Paradigm Diagnostics, Inc., a Delaware corporation ("Paradigm"), and Viomics, Inc., a Delaware corporation ("Viomics"), as follows: (i) an aggregate of 381,047 shares were issued to certain selling stockholders upon the closing of the Paradigm acquisition; (ii) up to an aggregate of 45,328 shares may be issuable to certain selling stockholders as payment of the Paradigm Holdback Amount (as defined herein); and (iii) up to an aggregate of 107,388 shares may be issuable to certain selling stockholders as payment of the Viomics Holdback Amount (as defined herein) as further described in this prospectus supplement under the heading "Selling Stockholders."

Our common stock trades on the Nasdaq Capital Market under the symbol "EXAS." On March 2, 2020, the last reported sale price of our common stock on the Nasdaq Capital Market was $77.43.

The selling stockholders may offer all or part of the shares registered hereby for resale from time to time directly to purchasers, through agents selected by the selling stockholders or to or through underwriters or dealers, at either prevailing market prices or at privately negotiated prices. If agents, underwriters or dealers are used in the sale of the shares by the selling stockholders, such agents, underwriters or dealers will be named and their compensation described in any applicable prospectus supplement.

INVESTING IN OUR SECURITIES INVOLVES RISKS. YOU SHOULD REVIEW CAREFULLY THE RISKS AND UNCERTAINTIES DESCRIBED UNDER THE HEADING "RISK FACTORS" ON PAGE S-7 OF THIS PROSPECTUS SUPPLEMENT.

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 supplement or the accompanying prospectus. Any representation to the contrary is a criminal offense.

The date of this prospectus supplement is March 4, 2020.

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ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement and the accompanying prospectus form part of a registration statement that we filed with the Securities and Exchange Commission (the "SEC") utilizing 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.

You should read this prospectus supplement together with the accompanying prospectus as well as additional information described under the heading "Where You Can Find More Information." You should rely only on the information contained or incorporated by reference in this prospectus supplement, the accompanying prospectus and any applicable "free writing prospectus." We have not authorized, and no selling stockholder has authorized, anyone else to provide you with different or additional information. No offer of the shares is being made in any jurisdiction where the offer or sale is not permitted.

You should not assume that the information in this prospectus supplement, the accompanying prospectus or any document incorporated by reference herein or therein is accurate as of any date other than their respective dates. Our business, financial condition, results of operations and prospects may have changed since those dates. You should carefully read the entire prospectus supplement and the accompanying prospectus, as well as the documents incorporated by reference herein and therein and any applicable "free writing prospectus" before making an investment decision.

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

SUMMARY

This summary highlights important features of this offering and the information included or incorporated by reference in this prospectus supplement. This summary does not contain all of the information that you should consider before investing in our common stock. You should read this entire prospectus supplement and the accompanying prospectus carefully, especially the "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" and the financial statements and related notes thereto contained herein or otherwise incorporated by reference hereto, before making an investment decision.

Business Overview

We are a leading global cancer diagnostics company. We have developed some of the most impactful brands in cancer diagnostics, and we are currently working on the development of additional tests for other types of cancer, with the goal of bringing new innovative cancer tests to patients throughout the world.

On November 8, 2019, we completed the acquisition of Genomic Health, Inc. ("Genomic Health"), a leading provider of genomic-based diagnostic tests that help to optimize cancer care, and its Oncotype IQ® Genomic Intelligence Platform comprised of its flagship line of Oncotype DX® gene expression tests.

Our Cologuard® Test

Colorectal cancer is the second leading cause of cancer deaths in the United States ("U.S.") and the leading cause of cancer deaths in the U.S. among non-smokers. In 2020 in the U.S. there are projected to be approximately:

- 148,000 new cases of colorectal cancer
- 53,000 deaths from colorectal cancer

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. 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 71 percent and 14 percent, respectively, compared to a 90 percent survival rate if the disease is diagnosed in stage 1. 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 that 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.

Changes in DNA methylation, and the occurrence of mutations, alter gene expression and other mechanisms for cell cycle regulation and differentiation. As a result, the affected cells continue to proliferate, often resulting in malignancies associated with colorectal cancer and pre-cancer. Hemoglobin is the protein complex responsible for transporting oxygen in red blood cells. During the progression of cancer, the probability of bleeding into the colon increases. The presence of hemoglobin,

released from red blood cells, can be detected in the stool. Using sDNA, Cologuard purifies, amplifies and detects increased levels of methylation, and presence of mutations, in specific genes. By combining these DNA indicators with a test for hemoglobin, Cologuard produces a multi-marker result effective for the detection of colorectal cancer and pre-cancerous adenomas.

In August 2014 the U.S. Food and Drug Administration ("FDA") granted premarket approval ("PMA") to Cologuard for use as a colorectal cancer screening test in adults 50 years of age and older who are at average-risk for colorectal cancer. Upon approval, Cologuard became the first and only FDA-approved sDNA non-invasive colorectal cancer screening test. In September 2019, the FDA expanded Cologuard's indication to include average-risk individuals ages 45-49. Cologuard is now indicated for average risk adults 45 years of age and older.

Our original PMA submission to the FDA for Cologuard included the results of our pivotal DeeP-C clinical trial that had over 10,000 patients 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%

We believe the competitive advantages of sDNA screening provide a significant market opportunity. There are nearly 106 million Americans between the ages of 45 and 85 who are at average-risk for colorectal cancer. At a three-year screening interval and an average revenue per test of approximately $500 this represents a potential $18 billion market for Cologuard, of which our current share is approximately 5.4 percent. We estimate that the FDA's recent expansion of Cologuard's indication to average-risk individuals ages 45-49 added approximately 19 million eligible people in the U.S.

Approximately an estimated 45 percent of Americans between the ages of 45 and 85 who are at average-risk for colorectal cancer are not up-to-date with screening according to the American Cancer Society's ("ACS") colorectal cancer screening guidelines. We believe Cologuard helps more people get screened for colorectal cancer. Internal studies have shown that nearly 50% of surveyed Cologuard users were previously unscreened for colorectal cancer.

Our Oncotype DX Tests

With our Oncotype IQ Genomic Intelligence Platform we are applying our world-class scientific and commercial expertise and infrastructure to lead the translation of clinical and genomic data into clinically actionable results for treatment planning throughout the cancer patient's journey, from diagnosis to treatment selection and monitoring. Our Oncotype IQ Genomic Intelligence Platform is currently comprised of our flagship line of Oncotype DX gene expression tests for breast, prostate and colon cancers, as well as Oncotype DX AR-V7 Nucleus Detect® test, a liquid-based test for advanced stage prostate cancer.

In the U.S., approximately 1.8 million new cancer cases are expected to be diagnosed in 2020 according to ACS. Cancer incidence and mortality are growing worldwide. In 2018, there were approximately 17 million newly diagnosed cancer cases and 9.5 million cancer-related deaths occurred worldwide. The most common types of cancer include breast, prostate, lung, colorectal and pancreatic. Cancer treatment decisions may include whether to perform surgery and whether to administer chemotherapy, radiation therapy or utilize other targeted therapies.

To treat cancer effectively, healthcare providers diagnose and gauge the stage of a patient's disease to determine the best course of therapy. Surgery, radiation therapy, and chemotherapy are commonly used as treatment options, with varying degrees of benefit and side effects that may not always justify the cost of the therapy or the physical and mental burden patients endure.

Historically, the key determinant used by healthcare providers in making cancer treatment decisions has been tumor pathology grade and stage, which is used to predict the likelihood of recurrence. Because tumor pathology grade and stage determinations are heavily dependent on visual assessment and human interpretation, healthcare providers and patients may make treatment decisions that rely on subjective and qualitative information and do not account for the molecular nature of the patient's cancer. As a result, many patients may be misclassified as high risk for disease recurrence when in fact they are low risk or, conversely, low risk for disease recurrence when they are high risk, resulting in over-treatment for some and under-treatment for others.

We believe our Oncotype DX tests provide information that has the following benefits:

- *Improved Quality of Treatment Decisions.* We believe our approach to genomic-based cancer analysis improves the quality of cancer treatment decisions by providing an individualized analysis of each patient's tumor that is correlated to clinical outcome, rather than solely using subjective, anatomic and qualitative factors to determine treatments. Our Oncotype DX tests for breast cancer, Ductal Carcinoma in Situ ("DCIS"), prostate cancer, and colon cancer have been analytically and clinically validated in multiple published studies. The Recurrence Score® results from our tests have been demonstrated to classify patients into recurrence risk categories different than classifications based primarily on clinical and pathologic features. Additionally, multiple decision impact studies conducted worldwide consistently show that the Recurrence Score result changes treatment decisions in more than 30% of patients. As a result, we believe our tests enable patients and healthcare providers to make more informed decisions about the risks and benefits of various treatments, and consequently design an individualized treatment plan.

- *Improved Health Economics of Cancer Care.* We believe that improving the quality of treatment decisions can result in significant economic benefits. For example, as described below, the results of a number of clinical studies have demonstrated that by using the Oncotype DX Breast Recurrence Score® test, physicians and patients can better evaluate treatment options, such as whether a patient will or will not benefit from chemotherapy, thereby improving the patient's prospects for better clinical outcomes by avoiding unnecessary chemotoxicities, secondary cancers, distant recurrences, and shortened survival and by saving the patient as well as the healthcare system significant costs.

International Business Background and Products

Prior to our combination with Genomic Health, we did not have international revenue. We now commercialize our Oncotype DX tests internationally through employees in Canada, Japan and six European countries, as well as through exclusive distribution agreements. We have provided our Oncotype DX tests in more than 90 countries outside of the United States. We do not offer Cologuard outside of the U.S.

Inclusion of our products in guidelines and quality measures will be critical to our international success. The Oncotype DX breast cancer test is recognized in international guidelines issued by the St. Gallen International Breast Cancer Expert Panel and European Society for Medical Oncology. In addition, the National Institute for Health and Care Excellence in England recommends the Oncotype DX breast cancer test for use in clinical practice to guide chemotherapy treatment decisions for certain patients with early-stage, N-, hormone receptor-positive, HER2 negative, invasive breast cancer, as well as certain patients with micrometastases. In June 2019, the German Federal Joint

Committee issued a positive reimbursement decision for our Oncotype DX Breast Recurrence Score test following a conclusion by the German Institute for Quality and Efficiency in Health Care that there is sufficient evidence supporting the ability of the test to guide breast cancer adjuvant chemotherapy decisions. Also, each of the Gynecologic Oncology Working Group in Germany and the Japan Breast Cancer Society updated their guidelines to recommend Oncotype DX as the only breast cancer gene expression test to predict chemotherapy benefit in early-stage, hormone receptor-positive invasive breast cancer.

We expect the international sales of our tests will be heavily dependent on the availability of reimbursement. In many countries, governments are primarily responsible for financing and establishing reimbursement for diagnostic tests. The majority of our international Oncotype DX test revenues come from direct payer reimbursement, payments from our distributors, and patient self-pay. We have obtained coverage for our invasive breast cancer test outside of the U.S., including coverage for certain patients in Canada, France, Spain, Germany, Italy, Ireland, Israel, Saudi Arabia, Switzerland, and the United Kingdom. We expect that broadening coverage and reimbursement for our Oncotype DX tests outside of the United States will take years.

Certain countries, such as China, have prohibitions against exporting tissue samples, which will limit our ability to offer our tests in those countries without local laboratories or a method of test delivery that does not require samples to be transported to our U.S. laboratory.

Pipeline Research and Development

Our research and development efforts are focused on developing new products and enhancing existing products to address new cancer areas and expand the clinical utility and addressable patient populations for our existing tests. These development efforts may lead to a variety of possible new products, including risk assessment, screening and prevention, early disease diagnosis, adjuvant and/or neoadjuvant disease treatment, metastatic disease treatment selection and patient monitoring.

Through our collaboration with Mayo Foundation for Medical Education and Research, we have successfully performed validation studies on multiple types of cancer using tissue, blood and other samples. We are currently focusing our research and development efforts on building a pipeline of potential future products and services with a focus on improving Cologuard's performance characteristics and on developing blood or other fluid-based ("liquid biopsy") tests. We expect to advance liquid biopsy through biomarker discovery and validation in tissue, blood, or other fluids.

Colon Cancer Screening

We are seeking opportunities to improve upon Cologuard's performance characteristics. For example, we are evaluating whether new biomarkers would increase specificity while maintaining sensitivity. If we could increase the specificity of Cologuard, we believe that would enhance its adoption as a front-line screening test. We are also evaluating ways that we might make Cologuard even easier for patients to use and opportunities for lowering the cost of providing Cologuard. In October 2019, we and Mayo presented at the American College of Gastroenterology's 2019 Annual Scientific Meeting findings from a blinded-case control study showing enhanced colorectal cancer and advanced adenoma detection using newly discovered methylation biomarkers and hemoglobin. To establish the performance of the novel multi-target stool DNA test, we recently launched the BLUE-C study, a multi-center, prospective study. We expect to enroll more than 10,000 patients 40 years of age and older in the BLUE-C study. The timing of any such enhancements to Cologuard is unknown and would be subject to FDA approval.

We are also working to develop a blood-based screening test for colorectal cancer.

Hepatocellular Carcinoma ("HCC") Test Development

We are currently seeking to develop a blood-based biomarker test to serve as an alternative to ultrasound and alpha-fetaprotein ("AFP") for use in HCC testing. HCC is the most common type of liver cancer. Our goal is to develop a patient-friendly test that performs better than the current standard of care. We are finalizing our HCC test development and plan to make the test available in the second half of 2020.

The ACS estimates that liver cancer would be diagnosed in 43,000 Americans and cause 30,000 deaths in 2020, approximately 90 percent of which would be HCC. Incidence and mortality rates are both increasing at approximately three percent per year. People who have been diagnosed with cirrhosis of the liver or Hepatitis B are at high risk of developing HCC. Evidence shows that HCC testing in these high-risk groups leads to earlier detection and improved outcomes. The NCCN and American Association for the Study of Liver Diseases guidelines recommend that these two groups be tested for HCC every six months using ultrasound and AFP. However, ultrasound and AFP are documented to have poor sensitivity for early stage cancer, which is the primary target of testing.

In November 2019, we released the results of a 443-patient study which demonstrated 80% sensitivity at 90% specificity with a novel combination of six blood-based biomarkers for HCC. The study also showed 71% sensitivity for early stage HCC at 90% specificity. The study compared performance to the AFP test, which demonstrated 45% sensitivity at 90% specificity for early stage HCC. Our HCC test has been granted Breakthrough Device designation by the FDA. The FDA's Breakthrough Devices program expedites development, assessment, and review processes to provide patients and healthcare providers with timely access to new technologies.

In Vitro Device ("IVD") Version of Oncotype DX Breast Cancer Test

We believe developing IVD versions of our Oncotype DX products that can be performed locally, rather than in our centralized Redwood City, California, laboratory, may open up additional international opportunities. We are currently developing an IVD version of the Oncotype DX Breast Recurrence Score test and may explore additional IVD versions of our Oncotype DX tests.

Development Studies for Oncotype DX Products

We may also conduct or fund clinical studies that could support additional opportunities for our products. For example, we may explore clinical studies to expand the use of genomic testing to address additional populations, including higher-risk patients.

Corporate Information

We were incorporated in the State of Delaware on February 10, 1995. Our corporate headquarters are located at 441 Charmany Drive, Madison, Wisconsin 53719. Our telephone number is (608) 535-8815. Our Internet website address is *www.exactsciences.com*. The information contained on, or that can be accessed through, our website is not a part of this prospectus.

THE OFFERING

Common Stock Offered by Selling Stockholders:	533,763 shares
Use of Proceeds:	Exact Sciences Corporation will not receive any proceeds from the sale of our shares of common stock by the selling stockholders.
Risk Factors:	Investing in our common stock involves risks. See "Risk Factors" and other information contained herein or otherwise incorporated by reference herein before deciding to invest in shares of our commons stock.
Nasdaq Capital Market Symbol:	Our common stock is listed on the Nasdaq Capital Market under the symbol "EXAS."

RISK FACTORS

Investing in our common stock involves risk. See the risk factors described in our Annual Report on Form 10-K for the fiscal year ended December 31, 2019 (together with any material changes thereto contained in subsequently 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 supplement and the accompanying 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.

FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus and the information incorporated by reference herein and therein 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 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, marketing and patient adherence efforts, expectations concerning payer reimbursement, the anticipated results of our product development efforts and the anticipated benefits of our acquisition of Genomic Health, Inc., including estimated synergies and other financial impacts. 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 our control. Our actual results and financial condition may differ materially from those indicated 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.

USE OF PROCEEDS

The selling stockholders will make offers and sales pursuant to this prospectus supplement and the accompanying prospectus. We will not receive any of the proceeds of such offerings. The selling stockholders will pay any underwriting discounts and commissions and expenses they incur for brokerage, accounting, tax or legal services, or any other expenses they incur in disposing of their shares. We will incur certain expenses in connection with the registration with the SEC of the shares of our common stock to be sold by the selling stockholders.

SELLING STOCKHOLDERS

This prospectus supplement relates to the resale of shares of our common stock issued or issuable to the selling stockholders pursuant to the acquisitions of Paradigm and Viomics as described below. The names of certain selling stockholders and information about their holdings and the offering are set forth below. The names of any additional selling stockholders and information about their holdings and any offering of the shares by them will be set forth in one or more additional prospectus supplements.

On March 3, 2020, we closed our acquisition of Paradigm, with Paradigm surviving as our wholly owned subsidiary. Certain of the selling stockholders named in the table below who are former stockholders and optionholders of Paradigm received an aggregate of 381,047 shares of common stock offered hereby as initial merger consideration for their ownership in Paradigm. In addition, we withheld 45,338 shares of common stock offered hereby payable as additional merger consideration to such former stockholders of Paradigm, after giving effect to certain reductions, on June 3, 2021 (the "Paradigm Holdback Amount").

Also on March 3, 2020, we closed our acquisition of Viomics, with Viomics surviving as our wholly owned subsidiary, for cash consideration. In addition, we withheld 107,388 shares of common stock offered hereby which may become payable as additional merger consideration to certain of the selling stockholders named in the table below who are former stockholders and optionholders of Viomics, after giving effect to certain reductions, in four equal installments on the first, second, third and fourth anniversaries of the closing of the Viomics acquisition (the "Viomics Holdback Amount").

The following table sets forth the name of each selling stockholder, the number of shares of our common stock beneficially owned by such selling stockholder before this offering (which assumes issuance of the maximum Paradigm Holdback Amount and the Viomics Holdback Amount, as applicable, payable to such stockholder), the number of shares of common stock to be offered for such selling stockholder's account and (if one percent or more) the percentage of common stock to be beneficially owned by such selling stockholder after completion of the offering. The number of shares of common stock owned are those beneficially owned, as determined under the rules of the SEC, and such information is not necessarily indicative of beneficial ownership for any other purpose. Under these rules, the selling stockholders' beneficial ownership includes any shares of our common stock as to which a person has sole or shared voting power or dispositive power and any shares of common stock which the person has the right to acquire within 60 days after March 3, 2020, and such shares are deemed to be beneficially owned and outstanding for computing the share ownership and percentage of the person holding such right, but are not deemed outstanding for computing the percentage of any other person. Except where we had knowledge of such ownership, the number presented in this column may not include shares held in street name or through other entities over which the selling stockholders have voting and dispositive power.

Unless otherwise set forth below, based upon information furnished to us by the selling stockholders, (i) the persons and entities named in the table have sole voting and sole dispositive power with respect to the shares set forth opposite the selling stockholder's name, subject to community property laws, where applicable, (ii) no selling stockholder had any position, office or other material relationship within the past three years with us or with any of our predecessors or affiliates, and (iii) no selling stockholder is a broker-dealer or an affiliate of a broker-dealer. The number of shares of common stock shown as beneficially owned before the offering is based on information furnished to us or otherwise based on information available to us at the time of the filing of the registration statement of which this prospectus forms a part. The number of shares beneficially owned after the offering assumes that all of the shares being offered by such selling stockholders are sold and assumes that no additional shares are purchased by such selling stockholders prior to the completion of this offering.

Information about the selling stockholders may change from time to time. Any changed information will be set forth in additional prospectus supplements or post-effective amendments, if

required by applicable law. As of February 19, 2020, there were 147,967,507 shares of our common stock outstanding.

Name of Selling Security Holder	Shares of Common Stock Beneficially Owned Prior to this Offering	Shares of Common Stock Registered Hereby	Shares of Common Stock Beneficially Owned upon Completion of this Offering**	Percentage of Common Stock Beneficially Owned upon Completion of this Offering
Ace Fund 19—San Diego, LLC	—	4,899	4,899	*
AltoIRA Empire Trust Custodian FBO Pradeep Mishra	—	488	488	*
Angel Capital Entrepreneur Fund 3 LLC	—	1,468	1,468	*
Anitar Investments LLC	—	3,918	3,918	*
Arvind Giowani	—	488	488	*
Ariane Kemkes	—	394	394	*
BlueStone Life Science Innovation & Technology Fund, LP	—	9,798	9,798	*
Bradley Clark	—	150	150	*
Brenda Curiel	—	56	56	*
Bret Gustafson	—	567	567	*
Bruce W. Irish	—	586	586	*
Bryan Brown	—	137	137	*
Carolyn Petit	—	59	59	*
Daniel Weber	—	72	72	*
David Friedman, Trustee David M. Friedman Trust dated 8/8/2007	—	244	244	*
David Mallery	—	99,691	99,691	*
David Neal	—	700	700	*
Duffer Family Revocable Trust	—	488	488	*
Elease Daugherty	—	137	137	*
Eric Thompson	—	1,543	1,543	*
Eric Williams	—	112	112	*
Erin Curley	—	364	364	*
Felicia Craciunescu	—	68	68	*
Felix Madrid	—	56	56	*
Genopraxis, LLC	—	488	488	*
Glen Weiss	—	949	949	*
Gore Range Capital Fund I LLC	—	11,757	11,757	*
Grant Schafer	—	50	50	*
Harry and Rosellen Papp Revocable Trust U/A DTD 02/09/1990	—	2,938	2,938	*
Hillary Winkel	—	234	234	*
James Eastin	—	283	283	*
Jeffrey C. Konicek	—	488	488	*
Jennifer Von Eschen	—	281	281	*
Jesus Banuelos	—	56	56	*
Joe Gatto	—	783	783	*
Johanna Gardner	—	68	68	*
John Friedman	—	586	586	*
Johnnie Wilson	—	68	68	*
Jon Eckles	—	68	68	*
Joseph Paulauskis	—	72	72	*

Name of Selling Security Holder	Shares of Common Stock Beneficially Owned Prior to this Offering	Shares of Common Stock Registered Hereby	Shares of Common Stock Beneficially Owned upon Completion of this Offering**	Percentage of Common Stock Beneficially Owned upon Completion of this Offering
Karen Rodriguez	—	47	47	*
Kari Kesterson	—	47	47	*
Krishnarao Tangella	—	1,068	1,068	*
Kyle Hogarth	—	1,556	1,556	*
Megan Pirie	—	59	59	*
Mesa Verde Venture Partners II LP	—	11,757	11,757	*
Michael Brown	—	488	488	*
Michael Castro	—	50	50	*
Michael Ostromecki	—	603	603	*
Michigan Health Corporation	—	78,167	78,167	*
New Juno, L.L.L.P.	—	488	488	*
NSV 2017 Opportunities Fund, LP	—	45,074	45,074	*
NSV 2018 Opportunities Fund, LP	—	22,536	22,536	*
NSV Investments I, LP	—	19,596	19,596	*
Northwest Ventures, LLC	—	488	488	*
Oberst Family Trust, dated 12-7-2005	—	488	488	*
OSF Healthcare System	—	29,396	29,396	*
Paras Gupta	—	488	488	*
Prairie Ventures, LLC	—	9,798	9,798	*
Prasad Sunkara	—	579	579	*
Rich Giambra	—	282	282	*
Rob Lozuk	—	59	59	*
Robert Armknecht	—	1,345	1,345	*
Robert Ramsey	—	50	50	*
Robert Tomec	—	50	50	*
Ryan Nelson	—	50	50	*
Scott Morris	—	31,690	31,690	*
Shankar Ram	—	503	503	*
Stephen Anthony	—	123	123	*
Stephen Gabe Rice	—	23	23	*
Taylor Walker	—	56	56	*
TC Schuttler Dynasty Trust U/A DTD 4/1/2011	—	4,899	4,899	*
The International Genomics Consortium	—	111,494	111,494	*
The Schilling Trust	—	3,918	3,918	*
Thomas Strilko	—	643	643	*
Trista Lange	—	46	46	*
Troy Shelton	—	9,022	9,022	*
Vanesa Romero	—	529	529	*
Veronica Fragoso	—	68	68	*
Ziad Mansour, Alice Mansour	—	488	488	*

* Less than 1%

** Assumes issuance of the maximum Paradigm Holdback Amount and the Viomics Holdback Amount, as applicable, payable to such stockholder.

PLAN OF DISTRIBUTION

The shares of our common stock covered by this prospectus may be offered and sold from time to time by the selling stockholders. The term "selling stockholders" includes donees, pledgees, assignees, transferees or other successors-in-interest selling shares received after the date of this prospectus from a selling stockholder as a gift, pledge, partnership distribution or other non-sale related transfer. The selling stockholders will act independently of us in making decisions with respect to the timing, manner and size of each sale. Such sales may be made on one or more exchanges in any market or trading facility on which the shares are traded, or in the over-the-counter market or otherwise, at fixed prices, at prices and under terms then prevailing or at prices related to the then current market price or in negotiated transactions. The selling stockholders may sell their shares by one or more of, or a combination of, the following methods:

- purchases by a broker-dealer as principal and resale by such broker-dealer for its own account pursuant to this prospectus;
- ordinary brokerage transactions and transactions in which the broker solicits purchasers;
- block trades in which the broker-dealer so engaged will attempt to sell the shares as agent but may position and resell a portion of the block as principal to facilitate the transaction;
- an over-the-counter distribution in accordance with the rules of The Nasdaq Stock Market LLC;
- through one or more underwritten offerings on a firm commitment or best efforts basis;
- in privately negotiated transactions;
- "at the market" or through market makers or into an existing market for the shares;
- through the distribution of the common stock by any selling stockholders to its partners, members or stockholders;
- through the writing or settlement of options or other hedging transactions, whether through an options exchange or otherwise, after the effective date of the registration statement of which this prospectus is a part; and
- any other method permitted pursuant to applicable law.

In addition, any shares that qualify for sale pursuant to Rule 144 may be sold under Rule 144 rather than pursuant to this prospectus supplement and the accompanying prospectus.

The aggregate proceeds to the selling stockholders from the sale of the shares of our common stock offered by them will be the purchase price of the shares less discounts or commissions, if any. We will not receive any of the proceeds from this offering.

To the extent required, this prospectus supplement and the accompanying prospectus may be amended or supplemented from time to time to describe a specific plan of distribution. In connection with distributions of the shares or otherwise, the selling stockholders may enter into hedging transactions with broker-dealers or other financial institutions. In connection with such transactions, broker-dealers or other financial institutions may engage in short sales of the common stock in the course of hedging the positions they assume with selling stockholders. The selling stockholders may also sell the common stock short and redeliver the shares to close out such short positions. The selling stockholders may also enter into option or other transactions with broker-dealers or other financial institutions which require the delivery to such broker-dealer or other financial institution of shares offered by this prospectus, which shares such broker-dealer or other financial institution may resell pursuant to this prospectus (as supplemented or amended to reflect such transaction). The selling stockholders may also pledge or grant a security interest in shares to a broker-dealer, other financial

institution or other person, and, upon a default such pledgee or secured parties may effect sales of the pledged shares pursuant to this prospectus (as supplemented or amended to reflect such transaction).

In effecting sales, broker-dealers or agents engaged by the selling stockholders may arrange for other broker-dealers to participate. Broker-dealers or agents may receive commissions, discounts or concessions from the selling stockholders in amounts to be negotiated immediately prior to the sale.

In offering the shares covered by this prospectus supplement and the accompanying prospectus, the selling stockholders and any broker-dealers who execute sales for the selling stockholders may be deemed to be "underwriters" within the meaning of the Securities Act in connection with such sales. Any profits realized by the selling stockholders and the compensation of any broker-dealer may be deemed to be underwriting discounts and commissions.

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

At the time a particular offer of shares is made, if required, an additional prospectus supplement will be distributed that will set forth the number of shares being offered and the terms of the offering, including the name of any underwriter, dealer or agent, the purchase price paid by any underwriter, any discount, commission and other item constituting compensation, any discount, commission or concession allowed or reallowed or paid to any dealer, and the proposed selling price to the public.

Certain agents, underwriters and dealers, and their associates and affiliates may be customers of, have borrowing relationships with, engage in other transactions with, and/or perform services, including investment banking services, for us or one or more of our respective affiliates in the ordinary course of business.

If any underwriters or agents are utilized in the sale of the shares in respect of which this prospectus supplement and the accompanying prospectus are delivered, we and the applicable selling stockholders will enter into an underwriting agreement or other agreement with them at the time of sale to them, and we will set forth in an additional prospectus supplement relating to such offering the names of the underwriters or agents and the terms of the related agreement with them.

In order to facilitate the offering of the shares, any underwriters may engage in transactions that stabilize, maintain or otherwise affect the price of the shares. Specifically, any underwriters may overallot in connection with the offering, creating a short position for their own accounts. In addition, to cover overallotments or to stabilize the price of the shares, the underwriters may bid for, and purchase, the shares in the open market. Finally, in any offering of the shares through a syndicate of underwriters, the underwriting syndicate may reclaim selling concessions allowed to an underwriter or a dealer for distributing the shares in the offering if the syndicate repurchases previously distributed shares in transactions to cover syndicate short positions, in stabilization transactions or otherwise. Any of these activities may stabilize or maintain the market price of the shares above independent market levels. Any such underwriters are not required to engage in these activities and may end any of these activities at any time.

LEGAL MATTERS

The validity of the securities offered hereby has been passed upon for us by K&L Gates LLP, Charlotte, North Carolina.

EXPERTS

The consolidated financial statements as of December 31, 2019 and 2018 and for each of the three years in the period ended December 31, 2019 and management's assessment of the effectiveness of internal control over financial reporting as of December 31, 2019 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.

WHERE YOU CAN FIND MORE INFORMATION

We file annual reports, quarterly reports, current reports and proxy statements and other information with the SEC under the Exchange Act. You may access and read our SEC filings, including the registration statement of which this prospectus supplement and the accompanying prospectus are a part and all of the exhibits to it, at the SEC's website located at www.sec.gov, which contains reports, proxy and information statements and other information regarding issuers that file electronically with the SEC.

Our web site is located at www.exactsciences.com. The information contained on, or that may be obtained from, our website is not, and shall not be deemed to be, a part of this prospectus supplement or the accompanying prospectus.

We have filed a registration statement, of which this prospectus supplement and the accompanying prospectus are a part, and related exhibits with the SEC under the Securities Act. This prospectus supplement and the accompanying prospectus, filed as part of the registration statement, do not contain all of the information set forth in the registration statement and its exhibits and schedules, portions of which have been omitted as permitted by the rules and regulations of the SEC. For further information about us and our common stock, we refer you to the registration statement and its exhibits and schedules.

We will provide, upon written or oral request, without charge to you, including any beneficial owner to whom this prospectus supplement and the accompanying prospectus is delivered, a copy of any or all of the documents incorporated by reference herein or therein other than the exhibits to those documents, unless the exhibits are specifically incorporated by reference into the information that this prospectus supplement or the accompanying 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) 535-8815.

INCORPORATION BY REFERENCE

This prospectus supplement and the accompanying prospectus "incorporate by reference" certain information that we have filed with the SEC under the Exchange Act. This means we are disclosing important information to you by referring you to those documents. We incorporate by reference into this prospectus supplement 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, 2019 filed with the SEC on February 21, 2020;
- Current Reports on Form 8-K filed with the SEC on January 31, 2020 and February 27, 2020;

- The information contained in the following sections of our definitive proxy statement for our 2019 Annual Meeting, filed with the SEC on April 30, 2019: "Information Concerning Directors and Nominees for Director," "Information Concerning Executive Officers," "Section 16(a) Beneficial Ownership Reporting Compliance," "Corporate Governance Principles, Board Matters and Non-Employee Director Compensation," "Compensation and Other Information Concerning Named Executive Officers," "Report of the Compensation and Management Development Committee," "Equity Compensation Plan Information," "Securities Ownership of Certain Beneficial Owners and Management," "Certain Relationships and Related Transactions," "Independent Registered Public Accounting Firm," and "Executive Compensation Tables"; and

- 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.

You should rely only on the information incorporated by reference or provided in this prospectus supplement and the accompanying prospectus. We have authorized no one to provide you with different information. You should not assume that the information in this prospectus supplement 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 supplement (other than any such documents or portions thereof that are furnished under Item 2.02 or Item 7.01 of Form 8-K, unless otherwise indicated therein, including any exhibits included with such Items) and prior to the termination of the offering will be deemed to be incorporated by reference in this prospectus supplement and will be a part of this prospectus supplement 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 supplement will be deemed to be modified or superseded for purposes of this prospectus supplement to the extent that a statement contained in this prospectus supplement or in any other subsequently filed document which also is or is deemed to be incorporated by reference in this prospectus supplement modifies or supersedes that statement. Any statement that is modified or superseded will not constitute a part of this prospectus supplement, except as modified or superseded.

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

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

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.

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

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

DESCRIPTION OF COMMON STOCK WE MAY OFFER

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

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

Authorized Capital

We currently have authority to issue 200,000,000 shares of our common stock, par value $0.01 per share. As of March 31, 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.

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

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.

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

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.