EXACT SCIENCES CORP
Form 10-K
February 21, 2019
Table of Contents

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10 K

ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the fiscal year ended: December 31, 2018
TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

Commission file number 001-35092

EXACT SCIENCES CORPORATION

(Exact name of registrant as specified in its charter)

DELAWARE	02 0478229
(State or other jurisdiction of incorporation or organization)	(IRS Employer Identification No.)
441 Charmany Drive, Madison, WI	53719
(Address of principal executive offices)	(Zip Code)

Registrant’s telephone number, including area code: (608) 284 5700

Securities registered pursuant to Section 12(b) of the Act:

Common Stock, $0.01 Par Value	The NASDAQ Stock Market LLC

Securities registered pursuant to Section 12(g) of the Act:

None

Indicate by check mark if the registrant is a well known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes No

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes No

Indicate by check mark whether the registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such report(s), and (2) has been subject to such filing requirements for the past 90 days. Yes No

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S T during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes No

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S K is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10 K or any amendment to this Form 10 K.

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non accelerated filer, a smaller reporting company or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company" and "emerging growth company" in Rule 12b 2 of the Exchange Act. (Check one):

Large accelerated filer	Accelerated filer	Non accelerated filer (Do not check if a smaller reporting company)	Smaller reporting company
			Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

Indicate by check mark whether the Registrant is a shell company (as defined in Rule 12b 2 of the Act). Yes No

The aggregate market value of the voting and non voting common equity held by non affiliates of the Registrant, as of the last business day of the Registrant's most recently completed second fiscal quarter was approximately $7,176,273,883 (based on the closing price of the Registrant's Common Stock on June 29, 2018 of $59.79 per share).

The number of shares outstanding of the Registrant's $0.01 par value Common Stock as of February 20, 2019 was 125,760,907.

DOCUMENT INCORPORATED BY REFERENCE

The registrant intends to file a definitive proxy statement pursuant to Regulation 14A within 120 days after the end of the fiscal year ended December 31, 2018. Portions of such proxy statement are incorporated by reference into Part III of this Form 10 K.

Table of Contents

EXACT SCIENCES CORPORATION

ANNUAL REPORT ON FORM 10 K

YEAR ENDED DECEMBER 31, 2018

TABLE OF CONTENTS

		Page No.
Part I		
Item 1.	Business	4
Item 1A.	Risk Factors	16
Item 1B.	Unresolved Staff Comments	38
Item 2.	Properties	38
Item 3.	Legal Proceedings	38
Item 4.	Mine Safety Disclosures	38
Part II		
Item 5.	Market for Registrant's Common Equity, Related Shareholder Matters and Issuer Purchases of Equity Securities	39
Item 6.	Selected Financial Data	40
Item 7.	Management's Discussion and Analysis of Financial Condition and Results of Operations	41
Item 7A.	Quantitative and Qualitative Disclosures about Market Risk	55
Item 8.	Financial Statements and Supplementary Data	57
Item 9.	Changes in and Disagreements with Accountants on Accounting and Financial Disclosure	105
Item 9A.	Controls and Procedures	105
Item 9B.	Other Information	105
Part III		
Item 10.	Directors, Executive Officers and Corporate Governance	106
Item 11.	Executive Compensation	106
Item 12.	Security and Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters	106
Item 13.	Certain Relationships and Related Transactions, and Director Independence	106
Item 14.	Principal Accountant Fees and Services	106
Part IV		
Item 15.	Exhibits and Financial Statement Schedules	107
Item 16.	Form 10-K Summary	111
SIGNATURES		112

Table of Contents

PART I

This Annual Report on Form 10 K contains forward looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, 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," "goal "estimate," "anticipate" or other comparable terms. All statements other than statements of historical facts included in this Annual Report on Form 10 K 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 payer 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 indicated 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 payers to cover our products and services and adequately reimburse us for such products and services; the amount and nature of competition from other cancer screening and diagnostic 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 pricing, coverage and reimbursement for our products and services, including without limitation as a result of the Protecting Access to Medicare Act of 2014; 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 ability to effectively utilize strategic partnerships, such as through our Promotion Agreement with Pfizer, Inc., and acquisitions; 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 described in the Risk Factors and in Management's Discussion and Analysis of Financial Condition and Results of Operations sections of this Annual Report on Form 10 K and our subsequently filed Quarterly Reports on Form 10-Q. 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.

Table of Contents

Item 1. Business

Overview

Exact Sciences Corporation (together with its subsidiaries, "Exact," "we," "us," "our" or the "Company") is a molecular diagnostics company 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 screening and diagnostics.

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. Each year in the U.S. there are approximately:

- 146,000 new cases of colorectal cancer
- 51,000 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. Of the more than 85 million people between the ages of 50 and 85, who are at average-risk for colorectal cancer in the U.S., 38 percent have not been screened according to current guidelines. Internal studies have shown that approximately 50% of Cologuard users were previously unscreened for colorectal cancer. 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 70 percent and 13 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 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. 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%

Table of Contents

We believe the competitive advantages of sDNA screening may provide a significant market opportunity. There are 85 million people in the U.S. between the ages of 50-85 who are at average risk for colorectal cancer. At a three-year screening interval and an average revenue per test of $500 this represents a potential $14 billion market for Cologuard, of which our current share is approximately four percent.

Our Cologuard Commercialization Strategy

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

Physicians and Patients

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 facilitate their ability to order the test. We focus on specific physicians based on a combination of Cologuard order history and ordering potential. We also focus on physician groups and larger regional and national health systems. We recently expanded our physician engagement and Cologuard marketing campaign through a Promotion Agreement (“Promotion Agreement”) with Pfizer, Inc. (“Pfizer”). The Promotion Agreement is discussed in more detail below.

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 U.S. 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, and Cologuard is the only version of FIT-DNA available in the U.S.

Many professional colorectal cancer screening guidelines in the U.S., including those of the American Cancer Society (“ACS”) and the National Comprehensive Cancer Network (“NCCN”), recommend regular screening using any of a variety of methods. Since 2008, joint colorectal cancer screening guidelines endorsed by the ACS have included sDNA screening technology as a screening option for the detection of colorectal cancer in average risk, asymptomatic individuals starting at age 50. In October 2014, the ACS updated its colorectal cancer screening guidelines to specifically include Cologuard as a recommended screening test and, as further discussed below, in May 2018 the ACS updated its colorectal cancer screening guidelines to recommend colorectal cancer screening begin at age 45 for people at average risk of the disease. In June 2016, the NCCN updated its Colorectal Cancer Screening Guidelines to add sDNA screening, at a once-every-three-years interval, to its list of recommended screening tests.

In May 2018, the ACS updated its guidelines to recommend colorectal cancer screening beginning at age 45, rather than 50, for people at average risk of the disease due to the rising incidence rate within the 45-49 year-old population. There are 21 million people who are within the ages of 45-49, and we estimate approximately 19 million of them are at average risk for colorectal cancer and eligible for screening. Cologuard is currently indicated for average risk individuals age 50 years or older. We intend to seek FDA approval to expand Cologuard's indication to people age 45 or older who are at average risk for colorectal cancer to align with the ASC updated guideline. We cannot be certain that FDA will grant such approval, or, if it does, when. Further, even if FDA does approve a label expansion, we cannot be certain that healthcare providers will prescribe, patients will use, or payers will reimburse Cologuard in the 45-49 age population.

In October 2016, the National Committee for Quality Assurance ("NCQA") included sDNA testing on a three-year interval as one of the methods permitted for colorectal cancer screening in the 2017 Healthcare Effectiveness Data and Information Set ("HEDIS") quality 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.

A critical part of the value proposition of Cologuard is its compliance program, which involves active engagement with patients and providers. This customer-oriented support activity is focused on encouraging and helping patients to complete Cologuard tests that have been ordered for them by their providers. We may undertake several activities to promote patient compliance including letters, text messages, emails, phone calls, and incentives such as gift cards.

After the launch of Cologuard, we initiated a significant public relations effort to engage patients in the U.S., and

Table of Contents

launched demographically-targeted direct-to-patient advertising campaigns in digital, social, print, and other channels. In 2016, we began a national television advertising campaign, with a majority of placements in national cable and syndicated programming widely viewed by our target patient demographic. In the second quarter of 2018, we extended our television advertising campaign to highlight the accuracy, ease of use, and commercial coverage of Cologuard. In 2019 we plan to increase our television advertising efforts, accelerate our investment in digital and social media, and embark upon other marketing initiatives designed to increase awareness of Cologuard.

We are focused on strengthening our Cologuard core business by increasing the size of our nationwide salesforce. We advanced this goal in August 2018 by entering into a Promotion Agreement with Pfizer. Under the terms of the Promotion Agreement, Pfizer will promote Cologuard and provide certain sales, marketing, analytical and other commercial operations support services. We and Pfizer committed in the Promotion Agreement to invest specified amounts in the advertising and promotion of Cologuard. We agreed to pay Pfizer a service fee based on incremental gross profits over specified baselines and pay Pfizer royalties for Cologuard related revenues for a specified period after the expiration or termination of the Promotion Agreement. The initial term of the Promotion Agreement runs through December 31, 2021, but may be terminated by either party at any time on or after February 21, 2020 upon six months' written notice to the other party.

Payers

Successful commercialization of our Cologuard test depends, in large part, on adequate reimbursement from government insurance plans, managed care organizations and private insurance plans.

In October 2014, CMS issued a National Coverage Determination ("NCD") for Cologuard following a parallel review process with the FDA. Medicare covers approximately half of patients in the current screening population for Cologuard. Cologuard was the first screening test approved by the FDA and covered by CMS through a parallel process. As 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).

The Clinical Laboratory Fee Schedule ("CLFS") for both 2018 and 2019 set the CMS reimbursement rate for Cologuard at $508.87. Under the Protecting Access to Medicare Act of 2014 ("PAMA"), payment rates for clinical diagnostic laboratory tests are calculated based on the volume-weighted median of private payer rates for each clinical diagnostic

laboratory test based on data submitted by certain applicable laboratories. The current CMS reimbursement rate was set based on the volume-weighted median of private payer rates for Cologuard for the period from January 1, 2016 to June 30, 2016. Based on current PAMA regulations, we expect that the current CMS reimbursement rate for Cologuard will remain in place until January 2021, and then will be reset based on the volume-weighted median of private payer rates for Cologuard during the data collection period from January 1, 2019 to June 30, 2019.

Pursuant to the Budget Control Act of 2011, Medicare payments, including Medicare's $508.87 reimbursement for Cologuard, became subject to a payment reduction of up to 2% due to implementation of the automatic expense reductions (i.e., a sequestration). The reduction is made to the total claims paid to plans and providers. Sequestration does not, however, rebase or re-establish the Medicare or Medicaid reimbursement rates.

In addition to Medicare reimbursement, we seek to secure favorable coverage and in-network reimbursement agreements from commercial payers. Most commercial payers have issued positive coverage decisions for Cologuard, and we have entered into contracts with several payers to include Cologuard as an in-network service. In-network agreements with payers have varying terms and conditions, including reimbursement rate, term and termination. From time to time in the ordinary course of our business, we may enter into new agreements, certain existing agreements may expire without renewal and certain other existing agreements may be terminated early by us or the third-party payer. We

Table of Contents

believe that commercial payers' reimbursement of Cologuard will depend on a number of factors, including payers' determination that it is: sensitive and specific for colorectal cancer; not experimental or investigational; approved or recommended by major organizations' guidelines; reliable, safe and effective; medically necessary; appropriate for the specific patient; and cost-effective. Reimbursement may also be affected by whether Cologuard is in-network for a given payer. Also, some payers may apply various medical management requirements, including a requirement that they give prior authorization for a Cologuard test before they are willing to pay for it. Other payers may perform post-payment reviews or audits, which could lead to payment recoupments. Medical management, such as prior authorizations and post-payment review or audits, may require that we, patients, or physicians provide the payer with extensive medical records and other information.

Coverage of Cologuard may also depend, in whole or in part, on whether payers 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 most health insurers to cover Cologuard without patient cost-sharing certain health insurers have disagreed and determined not to cover Cologuard and others may take that position in the future. It may be difficult for us or patients to enforce the ACA Mandate directly, and we may need to rely on states to take enforcement action, which they may choose not to do.

It is also possible that the ACA Mandate will be repealed, overturned or significantly modified in the future. Congress may modify or repeal all or part of the ACA, and any such modification or repeal may repeal or limit the ACA Mandate for preventive services. Additionally, the ACA has been the subject of various legal challenges, which, if ultimately successful, could overturn the ACA Mandate. In December 2018, a federal district court in Texas held that the ACA is unconstitutional and unenforceable. The court's decision is subject to appeal.

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 regarding certain state mandates, other insurers have disagreed. 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 maximize commercial payer coverage for Cologuard, including providing cost effectiveness data to payers to make the case for Cologuard reimbursement. We are focusing our efforts on large national and regional insurers and health plans that have affiliated health systems.

We believe quality metrics may influence payers' coverage and contracting decisions, as well as physicians' cancer screening procedures. Some government and private payers 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. Payers may look to quality measures, such as HEDIS and CMS Star Ratings, to assess quality of care. We believe Cologuard's inclusion in the HEDIS measures and Star Ratings measures positively impacts payers' willingness to reimburse Cologuard, as well as on healthcare providers' willingness to prescribe the test.

Our Clinical Laboratory and Manufacturing Facilities

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 55,000 square foot facility in Madison, Wisconsin. At our lab, we currently have the capacity to process approximately three million tests per year.

During the fourth quarter of 2017 we began construction of a new clinical lab facility in Madison, Wisconsin that is expected to be completed mid-2019. After the new clinical laboratory is operational, we expect our total lab capacity at both facilities will be approximately seven million tests per year by the end of 2019.

Table of Contents

We currently manufacture the Cologuard test in a facility in Madison, Wisconsin. As we expand the commercialization of Cologuard, we believe it will be necessary to expand our manufacturing capacity. Accordingly, we are in the process of building an additional manufacturing facility which we expect to complete in 2019. We are committed to manufacturing and providing medical devices and related products that meet customer expectations and applicable regulatory requirements. We adhere to manufacturing and safety standards required by federal, state, and local laws and regulations and operate our manufacturing facilities under a quality management system. We purchase certain components for our Cologuard test from third-party suppliers and manufacturers.

Future Product Opportunities

Enhance Cologuard

In May 2018, the ACS updated its guidelines to recommend colorectal cancer screening beginning at age 45, rather than 50, for people at average risk of the disease due to the rising incidence rate within the 45-49 year-old population. There are nearly 21 million people who are between the ages of 45-49, and we estimate approximately 19 million of them are at average risk for colorectal cancer and would be eligible for screening under the ACS guidelines. We plan to conduct clinical and other necessary work to gain FDA approval to expand Cologuard's indication to people between the ages of 45 and 49 who are at average risk for colorectal cancer.

In addition, 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.

The timing of any expansion of Cologuard's indication or of any such enhancements to Cologuard is unknown and would be subject to FDA approval.

Advance Liquid Biopsy

We also are focusing our research and development efforts on building a pipeline of potential future products and services with a focus on blood-based ("liquid biopsy") tests. We will continue to advance liquid biopsy through biomarker discovery and validation in tissue and blood. We have identified proprietary biomarkers for several cancers, including liver cancer and lung cancer. We have successfully performed validation studies on tissue samples for thirteen cancers and on blood samples for eight cancers.

The ACS estimates that liver cancer will be diagnosed in 42,000 Americans and cause 32,000 deaths in 2019, three-fourths of which will be hepatocellular carcinoma ("HCC"). Incidence and mortality rates are both increasing at approximately 3 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 ("AASLD") guidelines recommend that these two groups be tested for HCC every six months using ultrasound and the blood-based biomarker alpha-fetoprotein ("AFP"). However, ultrasound and AFP are documented to have poor sensitivity for early

stage cancer, which is the primary target of testing. We are currently seeking to develop a blood-based biomarker test to serve as an alternative to ultrasound and AFP for use in HCC testing, and our goal is to develop a patient-friendly test that performs better than this current standard of care. We are currently enrolling a case control study of at least 1,500 patients to finalize the development of our liver cancer test.

The ACS estimates that, in the U.S. in 2019, lung cancer will be diagnosed in 228,000 people and cause 143,000 deaths. Currently, more than half of lung cancer cases are diagnosed at an advanced stage, after symptoms appear, when the five-year survival rate is in the low single digits. We are currently seeking to develop 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”)

Table of Contents

or other scan. Such a test may help reduce the number of follow-up procedures, and thereby reduce costs and improve health outcomes.

Research and Development

Research and development costs account for a material portion of our operating expenses. As we seek to enhance Cologuard and expand our product pipeline by developing additional cancer screening and diagnostic tests, we expect that our research and development expenditures will continue to increase.

Competition

The U.S. market for colorectal cancer and pre-cancer screening is large, consisting of more than 85 million individuals between the ages of 50 and 85. If the screening population includes 45-49 year olds, as recommended by the ACS, the colorectal cancer screening market would increase by approximately 19 million people to approximately 104 million people. Given the large market for colorectal cancer screening, we face numerous competitors, some of which possess significantly greater financial and other resources and development capabilities than us. Our Cologuard test faces competition from procedure based detection technologies such as colonoscopy, flexible sigmoidoscopy, and "virtual" colonoscopy, a radiological imaging approach that visualizes the inside of the bowel by CT scan (spiral computerized axial tomography), as well as other common screening tests, such as the fecal occult blood test ("FOBT") and the fecal immunochemical test ("FIT"), and newer screening technologies such as pill-based imaging solutions like PillCam COLON, cleared by the FDA in February 2014, and C-Scan, which obtained a CE Mark in early 2019. Our competitors may also be developing additional methods of detecting colorectal cancer and pre-cancer that have not yet been announced.

In addition, some companies and institutions are developing liquid biopsy tests based on the detection of proteins, tumor cells, nucleic acids, epigenetic markers, or other biomarkers in the blood. These tests could represent significant competition for Cologuard and other tests we may develop. We are aware of at least 13 companies—Epigenomics AG, EDP Biotech Corporation, Freenome Inc., GRAIL, Inc., CellMax, Inc., Volition Diagnostics, Cambridge Epigenetix Limited, Nucleix Ltd., Singlera Genomics, DiaCarta, Genomictree, Bioprognos, and PapGene, Inc. — that have developed, or are developing, liquid biopsy tests for the detection of colorectal cancer. Epigenomics AG received FDA approval for its liquid biopsy screening test for colorectal cancer, Epi proColon, in April 2016, and began offering the test commercially in May 2016. We also are aware of at least two companies, DiaTech and Geneoscopy, that have launched outside the U.S., or are seeking to develop, stool-based colorectal cancer tests based on the detection of nucleic acids.

We believe other companies are also working on liquid biopsy tests using next generation sequencing or other technologies, and these tests could represent significant competition for Cologuard and other tests we may develop.

Notwithstanding that the market for colorectal cancer screening is highly competitive, we believe that Cologuard, as the first and only sDNA-based non-invasive colorectal cancer screening test on the market today, compares favorably to other available products and services. All other colorectal cancer detection methods in use today are constrained by some combination of poor sensitivity, poor compliance, and high cost. For example, colonoscopy requires advance dietary restrictions and bowel cleansing and can be uncomfortable, time consuming, hazardous, and expensive.

Colonoscopy requires sedation, potential lost time from work, and someone to drive the patient home from the procedure. A 2010 study shows that seven out of 10 people age 50 and older who were told they should get a colonoscopy did not do so primarily due to fears. Fecal blood testing, including FIT testing, suffers from poor sensitivity, with only a 74 percent detection rate for cancer and 24 percent detection rate for pre cancers. The blood based DNA tests currently available are also disadvantaged by relatively low sensitivity. Epigenomics AG has reported that the Epi proColon test has an overall cancer sensitivity rate of 68 percent, and only 59 percent for early-stage cancer. Additionally, FIT testing suffers from low adherence over time. One study published in the American Journal of Managed Care demonstrated that only three out of every 1,000 patients studied adhered to fecal test screening guidelines during a continuous 10-year observation period.

Beyond our Cologuard test, as we seek to develop other tests to detect cancer and pre-cancer, we expect to compete with a broad range of organizations in the U.S. and other countries that are engaged in the development, production and commercialization of cancer screening and diagnostic products and services. These competitors include:

Table of Contents

- biotechnology, diagnostic and other life science companies;
- academic and scientific institutions;
- governmental agencies; and
- public and private research organizations.

We may be unable to compete effectively against our competitors either because their products and services are superior or because they may have more expertise, experience, financial resources, or stronger business relationships. These competitors may have broader product lines and greater name recognition than we do. We have limited experience developing tests for detecting non-colorectal cancers and cannot guarantee that our research and development activities will be successful in developing any marketable testing products or services. Furthermore, even if we do develop new marketable products or services, our current and future competitors may develop products and services that are more commercially attractive than ours, and they may bring those products and services to market earlier or more effectively than us.

Seasonality

We are in the early stages of Cologuard's commercialization and are continuing to learn how seasonal factors may affect our business. Based on our experience to date, we expect some seasonal variations in our financial results due to a variety of factors, such as the year-end holiday period and other major holidays, vacation patterns of both patients and physicians, climate and weather conditions in our markets, seasonal conditions that may affect medical practices and provider activity, including for example influenza outbreaks that may reduce the percentage of patients that can be seen for preventive care such as colorectal cancer screening, and other factors relating to the timing of patient deductibles and co-insurance limits.

Government Regulation

Certain of our activities are subject to regulatory oversight by the FDA under provisions of the Federal Food, Drug, and Cosmetic Act ("FDCA") and regulations thereunder, including regulations governing the development, marketing, labeling, promotion, manufacturing, distribution, and export of diagnostic products. Our clinical laboratory facilities are subject to oversight by CMS pursuant to CLIA, as well as agencies in various states, including New York. We are subject to many other federal and state laws, including anti-fraud and abuse, anti-kickback and patient privacy. Failure to comply with applicable requirements can lead to sanctions, including withdrawal of products from the market, recalls, refusal to authorize government contracts, product seizures, exclusion from participation in federal and state healthcare programs, civil money penalties, injunctions, and criminal prosecution.

U.S. Food and Drug Administration

The FDA granted premarket approval ("PMA") for Cologuard in August 2014. Devices subject to FDA regulation must undergo premarket review prior to commercialization unless the device is exempt from such review. The regulations governing Cologuard's approval place substantial restrictions on how Cologuard is marketed and sold, specifically, by prescription only. In addition, as a condition of our FDA approval, we are required to conduct a post-approval study. A final report on this study is due to FDA in 2020. There can be no assurance that the results of this study will be satisfactory and will not cause the FDA to modify or withdraw our approval for Cologuard.

Additionally, manufacturers of medical devices must comply with various regulatory requirements under the FDCA and regulations thereunder, including, but not limited to, quality system regulations, unless they are exempt, facility

registration, product listing, labeling requirements, and certain post-market surveillance requirements. Entities that fail to comply with FDA requirements can be liable for criminal or civil penalties, such as recalls, detentions, orders to cease manufacturing, and restrictions on labeling and promotion, among other potential sanctions. In 2017, we recalled one of the components of our Cologuard test kit and circumstances may arise that cause us to recall other products or components used in connection with our Cologuard test.

We may develop new diagnostic products and services that are regulated by the FDA as medical devices. The regulatory review and approval process for medical devices can be costly, timely, and uncertain. This process may involve, among other things, successfully completing additional clinical trials and submitting a premarket clearance notice or filing a premarket approval application with the FDA. If premarket review is required by the FDA, there can be no assurance that our tests will be cleared or approved on a timely basis, if at all. In addition, there can be no assurance

Table of Contents

that the labeling claims cleared or approved by the FDA will be consistent with our current claims or adequate to support continued adoption of and reimbursement for our products. Ongoing compliance with FDA regulations could increase the cost of conducting our business, subject us to FDA inspections and other regulatory actions, and potentially subject us to penalties in the event we fail to comply with such requirements.

We may also develop diagnostic products or services that, under today's laws, would be regulated as laboratory developed tests ("LDTs") under CLIA. However, as noted below, the regulation of LDTs may be in flux, as the FDA retracted a proposal for increased LDT oversight in January 2017 and continues to apply enforcement discretion.

Laboratory Developed Tests ("LDTs")

LDTs are clinical laboratory tests that are developed and validated by a laboratory for its own use. Historically, LDTs have been regulated under CLIA while the FDA has exercised enforcement discretion and not required approvals or clearances for many LDTs performed by CLIA-certified laboratories. The FDA has traditionally chosen not to exercise its authority to regulate LDTs because LDTs were limited in number, were relatively simple tests, and were typically used to diagnose rare disease and uncommon conditions.

In October 2014, the FDA published two draft guidance documents describing a proposed risk-based framework under which the FDA might regulate LDTs. The FDA's draft framework proposed, among other things, premarket review for higher-risk LDTs, such as those that have the same intended use as FDA-approved or cleared diagnostics currently on the market. In November 2015, the FDA issued a report citing evidence for the need for additional regulation of LDTs and stated the FDA is continuing to work to finalize premarket review requirements for LDTs. However, in November 2016 the FDA announced it would not issue a final guidance for LDTs. In January 2017, the FDA issued a Discussion Paper on LDTs, which confirmed it would not finalize its guidance on the regulation of LDTs to allow more time for public discussion and time for the congressional authorizing committees to develop a legislative solution. It is unclear at this time if or when the FDA end enforcement discretion for LDTs. It is also unclear whether the FDA may decide to regulate certain LDTs on a case-by-case basis at any time. Action by the FDA to exercise enforcement discretion over LDTs, may materially impact our development and commercialization of LDTs.

Laboratory Certification, Accreditation and Licensing

We are also subject to U.S. and state laws and regulations regarding the operation of clinical laboratories. CLIA requirements and laws of certain states, including those of California, New York, Maryland, Pennsylvania, Rhode Island and Florida, impose certification requirements for clinical laboratories, and establish standards for quality assurance and quality control, among other things. CLIA provides that a state may adopt different or more stringent regulations than federal law and permits states to apply for exemption from CLIA if the state's laboratory laws are equivalent to, or more stringent than, CLIA. For example, the State of New York's clinical laboratory regulations, which have received an exemption from CLIA, contain provisions that are in certain respects more stringent than federal law. Therefore, as long as New York maintains a licensure program that is CLIA-exempt, we will need to comply with New York's clinical laboratory regulations in order to offer our clinical laboratory products and services in New York.

We have current certificates to perform clinical laboratory testing. Clinical laboratories are subject to inspection by regulators and to sanctions for failing to comply with applicable requirements. Sanctions available under CLIA and certain state laws include prohibiting a laboratory from running tests, requiring a laboratory to implement a corrective plan, and imposing civil monetary penalties. If we fail to meet any applicable requirements of CLIA or state law, that

failure could adversely affect any future CMS consideration of our technologies, prevent their approval entirely, and/or interrupt the commercial sal