EXACT SCIENCES CORP
Form 10-K
March 15, 2007

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

x ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the fiscal year ended: December 31, 2006

o TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

Commission File Number: 000-32179

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.)
100 Campus Drive, Marlborough, Massachusetts	**01752**
(Address of principal executive offices)	(zip code)

Registrant s telephone number, including area code: (508) 683-1200

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

Common Stock, $.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 o No x

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 o No x

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 x No o

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. x

Indicate by checkmark whether or the registrant is a large accelerated filer, an accelerated filer, or a non-accelerated filer. See definition of accelerated filer and large accelerated filer in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer o Accelerated filer x Non-accelerated filer o

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

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 $52,131,339 (based on the closing price of the Registrant s Common Stock on June 30, 2006 of $2.10 per share).

The number of shares outstanding of the Registrant s $.01 par value Common Stock as of March 9, 2007 was 26,756,918.

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, 2006. Portions of such proxy statement are incorporated by reference into Part III of this Form 10-K.

EXACT SCIENCES CORPORATION

ANNUAL REPORT ON FORM 10-K

YEAR ENDED DECEMBER 31, 2006

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PART I

Item 1. Business

This business section and other parts of this Annual Report on Form 10-K contain forward-looking statements relating to, among other things, our expectations concerning our commercial strategy, our marketing, sales and reimbursement efforts and their likely future success, our research and development efforts, regulatory compliance and the effectiveness and market acceptance of our technologies and LabCorp s PreGen-Plus test. Our forward-looking statements involve risk and uncertainties. Our actual results may differ significantly from the results discussed in the forward-looking statements. Factors that might cause such a difference include, but are not limited to, those set forth in Item 1A. Risk Factors and elsewhere in this Form 10-K.

Overview

EXACT Sciences Corporation is an applied genomics company that develops proprietary DNA-based technologies for use in the detection of cancer. We have selected colorectal cancer as the first application of our technologies. We have licensed certain of our patents, on an exclusive basis through August 2008, to Laboratory Corporation of America® Holdings (LabCorp®) in connection with a commercial testing service developed by LabCorp and marketed under the name PreGen-Plus™. LabCorp s sales of PreGen-Plus represent our primary source of revenue.

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

Today, professional guidelines, including those of the ACS, the American College of Gastroenterology, and the American Gastroenterological Association, recommend regular screening by a variety of methods including colonoscopy, flexible sigmoidoscopy and fecal occult blood testing, or FOBT, as well as combinations of some of these methods. Of those people for whom screening is recommended, many reject the option of colonoscopy which, while accurate as a means of detecting colorectal cancer, is invasive. Despite having been available as a screening modality for several years, colonoscopy has not been widely embraced by patients. Until the commercial launch of PreGen-Plus in August of 2003, the only completely non-invasive option for colorectal cancer detection had been FOBT without a digital rectal exam. FOBT, however, suffers from relatively low sensitivity, particularly in detecting the earliest stage, most curable cancers. In addition, FOBT screening tests require unpleasant stool sampling and stool manipulation by the patient, and certain FOBT screening tests also require dietary modifications. With the U.S. launch of PreGen-Plus by LabCorp, PreGen-Plus became the first commercially-available, completely non-invasive, DNA-based cancer screening test in the United States for the average risk population. In a study published in the December 23, 2004 issue of the *New England Journal of Medicine*, PreGen-Plus was shown to be four times more sensitive in detecting colorectal cancer than the most commonly used FOBT screening test on the market today, Hemoccult II®, to which it was compared in this study.

PreGen-Plus is offered commercially by LabCorp, the second largest commercial laboratory in the United States with more than 35 primary laboratories and over 1,700 patient service centers. LabCorp is the exclusive licensee, in the United States and Canada, of certain of our technologies utilized in PreGen-Plus through August 2008, followed by a non-exclusive license for the life of the licensed patents. LabCorp currently does not offer PreGen-Plus in Canada. LabCorp performs the PreGen-Plus test in its

laboratories, makes the test available through its sales force of more than 1,100 people and, by the terms of the license, pays us a royalty on each test reimbursed.

To date, LabCorp has paid us $30 million in upfront license fees and milestones associated with the license. In addition, LabCorp has committed to paying an additional $45 million in milestones and performance incentives in the event that certain third party approval and substantial performance levels are achieved. Between the commercial launch of PreGen-Plus in August 2003 and December 31, 2006, LabCorp has received over 12,500 patient samples for testing from physicians across the country, billed insurers and received payment from numerous third-party payors, including more than 350 health plans. None of these third party payors have yet issued formal policy approval for PreGen-Plus. Moreover, we do not expect that third party payors will issue formal policy approval for PreGen-Plus prior to any inclusion of stool-based DNA screening in the colorectal cancer screening guidelines of major guidelines organizations, or that PreGen-Plus will be broadly used by a payor s members prior to any such formal approval.

Background

Colorectal cancer is the third most common malignant disease and the second most frequent cause of cancer-related death in the United States, with more than 153,000 new cases and more than 52,000 deaths anticipated in 2007. We believe that many colorectal cancer deaths occur because people are not screened for colorectal cancer at all, or they use ineffective screening methods that either fail to detect the cancer or detect it at a later stage, when the five-year survival rate falls below 50%. Moreover, the number of people who die annually from the disease has remained materially unchanged over the last 20 years, despite the availability of multiple colorectal cancer screening options, all of which we believe fail to effectively meet the collective needs of patients, doctors and payors.

As reported in the February 3, 2005 issue of the *New England Journal of Medicine,* the tumor-node-metastasis, or TNM, system of the American Joint Committee on Cancer is now the most commonly used system for staging colorectal cancer and serves as a benchmark for predicting the likelihood of five-year survival. This staging system is described in the table below.

TNM Staging for Colorectal Cancer*

Stage	TNM Classification	Five-Year Survival %
I	T1-2, N0, M0	90
IIA	T3, N0, M0	60-85
IIB	T4, N0, M0	
IIIA	T1-2, N1, M0	25-65
IIIB	T3-4, N1, M0	
IIIC	T (any), N2, M0	
IV	T (any), N (any), M1	5-7

Primary Tumor (T)

TX: Primary Tumor cannot be assessed
Tis: Carcinoma in situ
T1: Tumor invades submucosa
T2: Tumor invades muscularis propria
T3: Tumor penetrates muscularis propria and invades subserosa
T4: Tumor directly invades other organs or structures or perforates visceral peritoneum

Nodal status (N)

NX: Regional lymph nodes cannot be assessed
N0: No metastases in regional lymph notes
N1: Metastases in one to three regional lymph nodes
N2: Metastases in four or more regional lymph nodes

Distant Metastases (M)

MX: Presence or absence of distant metastases cannot be determined
M0: No distant metastases dectected
M1: Distant metastases detected

* Source: Greene FL, Balch CM, Fleming ID, et al., eds. AJCC cancer staging handbook, 6th ed. New York: Springer, 2002.

Detection of pre-cancerous adenomas and colorectal cancer in its earliest stages increases the likelihood of survival and reduces the significant cost associated with treating late-stage colorectal cancer. Accordingly, the ACS recommends that the more than 87 million Americans age 50 and above undergo regular colorectal cancer screening with the methods endorsed by the ACS.

Our Solution

We believe that stool-based DNA detection in the general population offers an opportunity to increase screening rates and decrease mortality from colorectal cancer. Our stool-based DNA detection technology includes proprietary and patented technologies that isolate and analyze the trace amounts of human DNA that are shed into stool every day from the exfoliation of cells that line the colon. When colorectal cancer is present, a minute portion of the total isolated human DNA will represent DNA shed from cancerous or pre-cancerous lesions. Once the human DNA in the sample is isolated, stool-based DNA detection looks for specific mutations and other abnormalities in that DNA associated with colorectal cancer. A positive result from stool-based DNA detection does not necessarily mean that a patient has colorectal cancer. A positive result means that one or more of the genetic markers associated with colorectal cancer likely shows a mutation or abnormality. Under such circumstances, the clinical protocol is for the patient to then obtain a colonoscopy for confirmation. Moreover, a negative result from stool-based DNA detection does not mean that a person is free of colorectal cancer. Stool-based

DNA detection, like virtually all screening tests (including mammography, Prostate Specific Antigen, or PSA, and Papanicolaou smear, or PAP smear) also reports false negatives. See Clinical Studies below for specific information on stool-based DNA technology.

We believe that our proprietary methods and technologies have several advantages that can lead to increased patient compliance and decreased mortality, including:

Performance. We have conducted several clinical studies supporting the performance of stool-based DNA detection for colorectal cancer, including a 5,500 patient multi-center study, the results of which were published in the December 23, 2004 issue of the *New England Journal of Medicine*. Based on this study data, our bead-based stool-based DNA detection technology demonstrated sensitivity four times greater than the leading FOBT, Hemoccult II, currently the most common non-invasive screening method for colorectal cancer, and was more than four times as effective as Hemoccult II in this study in detecting cancer at its early stages, when survival rates approach 90%. The stool-based DNA screening test that was developed by LabCorp and that LabCorp is commercially offering today incorporates several technical improvements over the test that was used in the multi-center study, which we believe result in higher assay sensitivity than that seen in our multi-center study. Moreover, in a recent research study that was published in *Clinical Gastroenterology and Hepatology* in January 2007, our next-generation version of stool-based DNA screening technology, or Version 2, demonstrated sensitivity of 88% and specificity of 82% for the detection of colorectal cancer.

Simplicity and Convenience. Unlike current invasive screening and diagnostic methods, stool-based DNA detection requires no pre-examination preparation, invasive procedures or anesthesia, and a sample can be collected in the privacy of one s home. In addition, our post-market data indicates that more than half of the people surveyed who were screened with stool-based DNA detection had never been screened before, which we believe indicates that stool-based DNA detection can lead to greater patient screening compliance.

The Testing Process

Diagnostic tests typically require sample collection and preparation procedures as well as detection methods. The stool-based DNA testing process involves proprietary sample preparation, DNA isolation, and analytical techniques that apply genomics discoveries to the early detection of colorectal cancer.

Specimen Collection and Transportation. Certain of our patents relating to stool-based DNA screening for colorectal cancer are based on collecting a single whole stool sample in an easy, non-invasive manner. Utilizing a specially designed specimen container, samples can be collected in the privacy of an individual s home and then sent directly to the laboratory for processing using one of the many national couriers.

Representative Sampling. We have invented proprietary stool homogenization methods designed to ensure that the stool sample that is processed at the laboratory will contain uniformly distributed DNA throughout the portion of the sample being tested which, in turn, helps to ensure that the DNA in the stool sample is representative of the entire stool and colon.

DNA Extraction, Purification and Amplification. The isolation and amplification of human DNA found in stool is technically challenging because over 99% of DNA in stool is not human DNA, but is actually DNA from bacteria normally found in the colon. In addition, there are substances in stool that make the isolation and amplification of human DNA a difficult task. Proprietary technologies are used to allow for the reproducible isolation and amplification of the human DNA found in stool.

Cancer Detection Methods. Specialized methods for detecting and identifying genomic markers associated with colorectal cancer can be performed on existing instruments commonly available in clinical laboratories conducting molecular testing.

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Commercial Focus

Our goal is to become a market leader in the development and licensing of technologies for the early detection of cancer, beginning with the early detection of colorectal cancer. To accomplish this goal, we are pursuing a strategy with respect to our technologies that includes the following components:

Pursue commercial introduction of next-generation stool-based DNA screening technology. In a recent research study that we conducted, Version 2 demonstrated sensitivity of 88% and specificity of 82% for the detection of colorectal cancer. The blinded Version 2 research study was designed to test the efficacy of technological advances to enhance colorectal cancer detection in stool. Although the specificity result in the Version 2 study was lower than our previous studies, in which the specificity exceeded 90%, we believe that the significant improvement in sensitivity compared to our prior studies, including our 5,500 patient multi-center study, will provide the basis to pursue commercial introduction of Version 2 in the future. This study involved the blinded analysis of post-colonoscopy collected stool samples from individuals whose colonoscopy results were positive for colorectal cancer. By contrast, our multi-center study, published in the *New England Journal of Medicine* in 2004, was comprised of pre-colonoscopy cancer samples from an asymptomatic population. The Version 2 research study was published in January 2007 in the journal of *Clinical Gastroenterology and Hepatology*.

While it is not yet clear to us when Version 2 of our technology will be made commercially available, our future plans with regard to Version 2 may include seeking the FDA s agreement that Version 2 qualifies as a homebrew testing service, seeking FDA clearance or approval on Version 2 in its assay form, and/or working alone or with a partner to develop an FDA-approved in vitro diagnostic testing kit for colorectal cancer screening, all of which may require additional studies of the Version 2 technology. We may also seek to offer Version 2 as a homebrew testing service out of our own laboratory, rather than having this more advanced technology utilized solely by LabCorp in its homebrew testing service. Offering Version 2 ourselves as a homebrew testing service would require LabCorp s approval as they currently are the exclusive licensee of our stool-based DNA screening technology for this type of diagnostic service.

Obtain inclusion of stool-based DNA screening in national colorectal cancer screening guidelines. Today, professional guidelines recommend screening by a variety of methods including colonoscopy, flexible sigmoidoscopy and FOBT. In general, the guidelines range from the use of colonoscopy every ten years to the use of FOBT annually. Inclusion in screening guidelines is, in our view, among the important preconditions to a test s broad acceptance and commercial use in the market as both physicians and payors frequently follow such guidelines in embracing new technologies. Outlined below is a summary of key organizations with responsibility for developing and publishing colorectal cancer screening guidelines, the relationships between those key organizations and, to our knowledge, the timing of when those organizations typically issue guideline updates.

The U.S. Multisociety Task Force on Colorectal Cancer, a consortium of several organizations including representatives of the American College of Gastroenterology, American Gastroenterological Association, American Society for Gastrointestinal Endoscopy and the American College of Physicians/Society of Internal Medicine (the MSTF-CRC), issued formal colorectal cancer screening guidelines that were endorsed by the ACS in 1997 and 2003. Since that time, the ACS joined with the MSTF-CRC (the ACS/MSTF-CRC) to begin work on a further update of the colorectal cancer screening guidelines. We view inclusion in the guidelines of the ACS/MSTF-CRC as being of primary importance to the commercialization of stool-based DNA screening. We do not expect that there will be a screening guidelines decision issued by the ACS/MSTF-CRC before the end of June 2007, at the earliest. In the event stool-based DNA screening is included in screening guidelines, it may still take several months before this information becomes published and is usable from a sales and marketing perspective. Also, if the guidelines recommendation relates to a particular version of our stool-based DNA screening technology only, and not to stool-based DNA screening in general, or otherwise limits stool-based DNA colorectal cancer screening among the choices offered, this may further limit the test s ability to gain market acceptance and broad adoption.

In addition to its participation in the ACS/MSTF-CRC, and independent of those efforts, the ACS annually publishes its Guidelines for the Early Detection of Cancer in its journal, *CA: A Cancer Journal for Clinicians*. This annual article typically includes an overview of current screening guidelines for all cancers and a review of any guideline revisions made during the prior calendar year, if any. Accordingly, we do not expect stool-based DNA screening to be included in those recommendations and our focus remains on the ACS/MSTF-CRC guideline update relating to stool-based DNA screening for colorectal cancer, which we expect will occur some time after the publication of the ACS s Guidelines for the Early Detection of Cancer appearing in *CA: A Cancer Journal for Clinicians.*

Obtain regulatory clearance of stool-based DNA screening. Current and future versions of stool-based DNA testing, including Version 2, may require FDA clearance or approval. If the FDA determines that our stool-based DNA testing technology, in whole or in part, requires premarket clearance or approval, commercial sales of PreGen-Plus could be delayed, halted or prevented and enforcement action could be initiated which could involve criminal or civil penalties. In addition, the FDA s position on this could negatively affect our operations either through regulation or new enforcement initiatives directed at LabCorp or EXACT. Further, the FDA may not approve of certain sales and marketing initiatives of EXACT, which could negatively affect our ability to build awareness around stool-based DNA testing.

Leverage LabCorp s large sales force. LabCorp is the second largest commercial laboratory in the country and processes over 370,000 patient specimens daily through its system of more than 36 primary laboratories and over 1,700 patient service centers across the United States. LabCorp s large sales force of `more than 1,100 people is devoted to selling a wide range of diagnostic tests to physicians across all specialties. As a result of discussions with the FDA regarding the regulatory status of PreGen-Plus, we have agreed to limit our sales and marketing efforts primarily on the following constituents: thought leaders and third party payors, including self-insured employers, managed care organizations, and the technology assessment groups within these organizations. Accordingly, we intend to leverage LabCorp s sales force to market PreGen-Plus to physicians. We believe that an important element to the successful commercialization of PreGen-Plus is the inclusion of stool-based DNA testing in colorectal cancer screening guidelines of the ACS/MSTF-CRC.

Obtain formal acceptance of stool-based DNA screening for reimbursement by Medicare and other third-party payors. Our reimbursement strategy consists primarily of working with LabCorp to educate large managed care organizations and large self-insured employers about the clinical benefits and cost-effectiveness of using stool-based DNA screening for colorectal cancer. We believe that both the publication of our multi-center study results in the *New England Journal of Medicine* in December 2004 and cost-effectiveness study results regarding stool-based DNA screening will aid in our efforts to gain reimbursement for the test. Accordingly, on December 29, 2004 we submitted our application for a National Coverage Determination to the Centers for Medicare and Medicaid Services, or CMS, for inclusion into the Medicare program. CMS has not approved stool-based DNA colorectal cancer screening for payment, has not yet accepted our request for a National Coverage Determination and has sought additional information regarding PreGen-Plus, which has delayed our application s acceptance. CMS will not deem our application complete until CMS is satisfied that it has received all necessary information to deem the application complete. CMS may determine that we and LabCorp have not provided the necessary information to CMS in a timely manner, if at all, or in a manner acceptable to CMS. After CMS is satisfied that it has received all information necessary for its evaluation of PreGen-Plus, CMS may accept the National Coverage Determination application, deeming it complete, or it may reject the application and request additional information or simply reject it outright. The timing of any acceptance of the National Coverage Determination application or any subsequent coverage decision by CMS is not within our control. We would not expect CMS to make a coverage decision sooner than nine months from the date of any acceptance of the National Coverage Determination application.

Broader diagnostic focus. We expect to continue our research and development efforts to validate and optimize our colorectal cancer screening technology. We are currently evaluating other opportunities in the staging, monitoring and prognosis of colorectal cancer.

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Clinical Studies

Stool-based DNA testing has been the subject of extensive research and clinical studies. In numerous studies to date, the performance of our stool-based DNA technology has been examined in thousands of tissue and stool samples. In a recent published study, Version 2 of our stool-based DNA screening technology demonstrated sensitivity of 88% and specificity of 82% for detecting colorectal cancer. While previous published studies for stool-based DNA screening have generally shown specificity above 90%, the specificity results in the Version 2 study were closer to 80%, a performance metric that may not be deemed clinically or commercially acceptable. The blinded study was designed to test the efficacy of technological advances to enhance colorectal cancer detection in stool. This study involved the analysis of 40 post-colonoscopy collected cancer samples from individuals whose colonoscopy results were positive for colorectal cancer. By contrast, our multi-center study in 2004, published in the *New England Journal of Medicine*, was comprised of 31 cancer samples prior to colonoscopy from an asymptomatic population.

In addition to several smaller clinical studies designed to measure the sensitivity and specificity of stool-based DNA testing in detecting colorectal cancer, the performance of the original version of our stool-based DNA testing technology was compared to the most widely-used FOBT in a large multi-center study that enrolled approximately 5,500 average-risk, asymptomatic patients from more than 80 sites across the United States. The study was designed to determine whether stool-based DNA testing was clinically superior to Hemoccult II®, an FOBT that is currently the most widely used non-invasive colorectal cancer screening test. The primary endpoint of this study was achieved with statistical significance, with a p-value of less than 0.003. Results from the study, which were published in the *New England Journal of Medicine* in December 2004, indicated that stool-based DNA testing was four times more sensitive than Hemoccult II® in the study in detecting colorectal cancer (52% for stool-based DNA testing versus 13% for Hemoccult II®), and more than four times more sensitive in detecting colorectal cancer in its earliest, most curable stages (57% for stool-based DNA testing versus 13% for Hemoccult II®). There was no difference in specificity between stool-based DNA testing and this FOBT, with both tests demonstrating a specificity of approximately 95%.

Sensitivity and specificity results from our clinical studies that have been published are summarized in the table below. The results of these studies may not be directly comparable as these studies were conducted across a variety of patient populations and clinical settings and employed varying sample collection protocols. Moreover, the clinical studies disclosed below do not include any non-published studies regarding stool-based DNA testing, the results of which may differ significantly from those set forth below.

Technology & Study Name	Year Completed / Published	Number of Cancer Samples Analyzed	Number of Genetic Markers	DNA Capture Technology	DNA Stabilization Buffer Used (1)