OncoCyte Corp
Form 10-K
February 27, 2017

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, 2016

OR

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

For the transition period from_____ to _____

Commission file number 1-37648

OncoCyte Corporation
(Exact name of registrant as specified in its charter)

California	27-1041563
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)

1010 Atlantic Avenue, Suite 102
Alameda, California 94501
(Address of principal executive offices) (Zip Code)

Registrant's telephone number, including area code (510) 775-0515

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

Title of each class	Name of exchange on which registered
Common Stock, no par value	NYSE MKT

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 reports), 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 (§ 232.405 of this chapter) 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 (§229.405 of this chapter) 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, or a smaller reporting company. See the definitions of "large accelerated filer," "accelerated filer" and "smaller reporting company" in Rule 12b-2 of the Exchange Act.

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

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act): Yes No

The approximate aggregate market value of shares of voting common stock held by non-affiliates computed by reference to the price at which shares of common stock were last sold as of June 30, 2016 was $14.7 million. Shares held by each executive officer and director and by each person who beneficially owns more than 5% of the outstanding common stock have been excluded in that such persons may under certain circumstances be deemed to be affiliates. This determination of affiliate status is not necessarily a conclusive determination for other purposes.

As of February 17, 2017, there were outstanding 29,361,616 shares of common stock, no par value.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's Proxy Statement for its 2017 Annual Meeting of Shareholders are incorporated by reference in Part III

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PART I

Certain statements contained herein are forward-looking statements, within the meaning of the Private Securities Litigation Reform Act of 1995, including, but not limited to, statements pertaining to future financial and/or operating results, future growth in research, technology, clinical development, and potential opportunities for OncoCyte, along with other statements about the future expectations, beliefs, goals, plans, or prospects expressed by management constitute forward-looking statements. Any statements that are not historical fact (including, but not limited to statements that contain words such as “will,” “believes,” “plans,” “anticipates,” “expects,” “estimates”) should also be consider to be forward-looking statements. Forward-looking statements involve risks and uncertainties, including, without limitation, risks inherent in the development and/or commercialization of potential products, uncertainty in the results of clinical trials or regulatory approvals, need and ability to obtain future capital, and maintenance of intellectual property rights. Actual results may differ materially from the results anticipated in these forward-looking statements and as such should be evaluated together with the many uncertainties that affect the businesses of OncoCyte, particularly those mentioned in the cautionary statements found in OncoCyte’s filings with the Securities and Exchange Commission. OncoCyte disclaims any intent or obligation to update these forward-looking statements.

References to “OncoCyte,” “our” or “us” mean OncoCyte Corporation.

The description or discussion, in this Form 10-K, of any contract or agreement is a summary only and is qualified in all respects by reference to the full text of the applicable contract or agreement.

INDUSTRY AND MARKET DATA

This Annual Report on Form 10-K contains market data and industry forecasts that were obtained from industry publications, third party market research and publicly available information. These publications generally state that the information contained therein has been obtained from sources believed to be reliable. While we believe that the information from these publications is reliable, we have not independently verified such information.

This Annual Report on Form 10-K also contains estimates and other statistical data made by independent parties and by us relating to market size and growth and other data about our industry. We obtained the industry and market data in this Report from our own research as well as from industry and general publications, surveys and studies conducted by third parties, some of which may not be publicly available. Such data involves a number of assumptions and limitations and contains projections and estimates of the future performance of the industries in which we operate that are subject to a high degree of uncertainty. We caution you not to give undue weight to such projections, assumptions and estimates.

PRELIMINARY NOTE ABOUT OWNERSHIP OF OUR COMMON STOCK

As of February 17, 2017, we had 277 shareholders of record and there were 29,361,616 shares of our common stock outstanding, of which 14,674,244 shares were held by our parent BioTime, Inc. ("BioTime"). The shares held by BioTime account for less than 50% of our common stock outstanding as a whole. Accordingly, effective February 17, 2017, we are a no longer a consolidated subsidiary of BioTime. See Note 10 of our financial statements included elsewhere in this Annual Report.

REVERSE STOCK SPLIT

On November 18, 2015, OncoCyte effected a 1-for-2 reverse stock split of its common stock. All references to common stock, warrants, and options to purchase common stock, and all per share data and related information, including the price at which shares of common stock have been sold or may be issued, have been retroactively adjusted, where applicable, to reflect the reverse stock split of OncoCyte common stock as if it had occurred at the

beginning of the earliest period presented.

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Item 1. Business

Overview

Our mission is to develop highly accurate, easy to administer, non-invasive molecular diagnostic tests to improve the standard of care for cancer diagnosis to better meet the needs of patients, physicians and payers. Our initial focus will be confirmatory diagnostics, utilizing novel liquid biopsy technology, for use in conjunction with imaging to confirm initial suspicious imaging results such as lung nodules and breast lumps within certain oncology indications. In addition, we may develop screening diagnostics as potential replacements for screening imaging protocols that do not meet the needs of patients, health care providers or payers. For some indications, we may also pursue the probability of recurrence of a specific cancer through the development of prognostics; or companion diagnostics that help a physician determine which therapy is the optimal treatment for the patient.

Our initial liquid biopsy diagnostic tests will be confirmatory diagnostics and are being developed to reduce false positive results associated with current diagnostic protocols. These new diagnostic tests are intended to:

- Reduce unnecessary and sometimes risky procedures, as well as lower the cost of care through the avoidance of more expensive diagnostic procedures, including invasive biopsy and cystoscopic procedures

- Improve the quality of life for cancer patients by reducing the anxiety associated with non-definitive diagnoses; and

- Improve health outcomes through avoidance of unnecessary invasive procedures

We are currently developing diagnostic tests for three types of cancer: lung cancer, breast cancer, and bladder cancer. Our strategic focus is to develop diagnostic tests in areas of high unmet need.

We were incorporated in 2009 in the state of California. Our principal executive offices are located at 1010 Atlantic Avenue, Suite 102, Alameda, California 94501. Our telephone number is (510) 775-0515.

Business Strategy

Our strategy is to identify medical indications where current diagnostic technology is not meeting the needs of patients, physicians, or payers due to poor early detection and/or a large number of false positives. The current standard of care requires patients to endure unnecessary, costly and risky additional confirmatory procedures. By focusing on what we believe to be the biggest unmet needs with manageable technological hurdles and potentially rapid times to market we believe our strategy is an efficient and risk-balanced use of capital and human resources.

Unmet need, as we see it, can be defined from the physician and payer perspective as low five year survival rates and as low specificity or high numbers of false positive test results. Oncology indications that fit these parameters include lung and breast cancer, as can be seen in the following graphic. Additionally, our strategy is to focus on indications where competition is low, a specialty sales force can be leveraged and that do not require the presence of a large primary care sales force.

We are developing liquid biopsy (i.e. blood and urine based) molecular cancer diagnostics utilizing a discovery platform that focuses on identifying genetic markers expressed in specific types of cancer. The diagnostic markers we have discovered thus far may address unmet needs in cancer diagnostic indications that have a strong potential to generate short- to mid-term revenues. Our approach is based on focusing on unmet medical needs, large market sizes and ease of use of the product.

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Our current development strategy for cancer diagnostic tests is to develop, evaluate and validate specific diagnostics using methods of detecting proteins, messenger RNA ("mRNA") or micro RNA ("miRNA"). We believe that this approach allows us to have a broader look into the genetic markers that differentially express in cancer. Differential expression means that we are looking for proteins, mRNA or miRNA that are present in bodily fluids more often or less often when the patient has a specific type of cancer present in their body as compared to patients with no cancer. These elements in the bodily fluids are referred to as biomarkers. Our development strategy will be matched to our market planning strategy to determine which:

·Diagnostic tests to prioritize in our development program;

·Diagnostic tests we should market ourselves;

·Diagnostic tests we should co-market through an alliance with one or more other companies; and

·Diagnostic tests we should out-license to third parties for development and/or commercialization.

Additional Information

We are an "emerging growth company" as defined in the Jumpstart Our Business Startups Act of 2012. We will remain an "emerging growth company" until the earliest of (i) the last day of the fiscal year in which we have total annual gross revenues of $1.0 billion or more; (ii) the last day of our fiscal year following the fifth anniversary of the first sale of our common equity securities pursuant to an effective registration statement under the Securities Act of 1933, as amended (the "Securities Act"); (iii) the date on which we have issued more than $1.0 billion in nonconvertible debt during the previous three years; or (iv) the date on which we are deemed to be a large accelerated filer under the rules of the Securities and Exchange Commission, or the SEC. We refer to the Jumpstart Our Business Startups Act of 2012 herein as the "JOBS Act," and references herein to "emerging growth company" shall have the meaning associated with it in the JOBS Act.

As an emerging growth company, we may take advantage of specified reduced disclosure and other requirements that are otherwise applicable, in general, to public companies that are not emerging growth companies. These provisions include:

·Reduced disclosure about our executive compensation arrangements;

·No non-binding shareholder advisory votes on executive compensation or golden parachute arrangements; and

·Exemption from the auditor attestation requirement in the assessment of our internal control over financial reporting.

We may take advantage of these exemptions for up to five years or such earlier time that we are no longer an emerging growth company.

Diagnostic Tests

Based on substantial unmet needs, large markets, and data generated thus far from patient serum (blood) or urine screening, we are focusing our efforts on biomarkers associated with lung, breast and bladder cancers. Our approach is based on utilizing detectable amounts of cancer-associated biomarkers in patients with early-stage disease. Our identification of certain combinations of biomarkers in lung, breast and bladder cancer as well as clinician and payer feedback on unmet need has led us to identify promising initial indications and target analytes.

The relative ease of administering a liquid biopsy diagnostic and cost savings due to the elimination of unnecessary costlier and invasive surgical biopsy procedures, we believe, will make liquid biopsy diagnostic tests useful as routine tests that could be performed in men and women of any age and at any desired frequency in conjunctions with normal screening procedures to detect lung, breast or bladder cancer. If successful, our tests will initially reduce diagnosis uncertainty and eliminate unnecessary down-stream procedures resulting from indeterminate low dose computed tomography (“LDCT”), mammography, or cytology results.

We intend to initially develop and market a lung cancer diagnostic test in the United States before seeking regulatory approvals required to market the diagnostic test in other countries. The lung cancer test to be developed will be a blood confirmatory test for cancer biomarkers, which will be used in conjunction with LDCT for patients with indeterminate pulmonary nodules to help clinicians triage patients for follow-up procedures. The test will be regulated under the Clinical Laboratory Improvements Amendment (“CLIA”) as a laboratory diagnostic test or "LDT". We may also pursue approvals from the United States Food and Drug Administration (the “FDA”) or through the European Directive on in vitro diagnostics (“IVDs”) for any IVDs that we may develop.

We have begun establishing a CLIA laboratory in Alameda, California. Work that has been completed as of January 30th 2017 includes ordering and installation of necessary equipment needed for a potential launch and hiring of quality assurance and laboratory personnel. We currently plan to seek certification for our laboratory during the second quarter of 2017. This certification, along with additional certifications that we will seek over the next 18 months, may potentially allow us to offer our initial lung cancer test in all 50 states.

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Types of Diagnostic Use

Once we have completed development of a liquid biopsy diagnostic test and receive certification of our CLIA lab, we may commence marketing that diagnostic test for one or more specific kinds of use which relate to the kind of diagnostic evaluation that a physician is performing for a patient. Our diagnostics may have one or more of four different types of use depending on the type of cancer and the performance of the diagnostic. These intended uses include:

- Prognostic diagnostics – diagnostics used to predict the probability of a patient developing certain kinds of cancer. An example of this test is a BRCA test, which gives a probability of a women developing breast or ovarian cancer

- Screening diagnostics – screening diagnostics would replace or be used as an alternative to existing screening procedures. A screener diagnostic for breast cancer could be used as an alternative to mammograms for all women, or yearly mammograms and MRIs for women with a family history of breast cancer, BRCA mutations or dense breast tissue. This test could become part of a routine annual or other periodic physical examination;

- Confirmatory diagnostics – confirmatory diagnostics are used in conjunction with a current standard of care screening procedure. For example, our lung confirmatory diagnostic would be used in conjunction with LDCT to confirm a suspicious nodule by yielding a secondary suspicious versus benign result. In the case of a benign result, the patient would not need additional invasive procedures to determine the presence of cancer. In the case of a suspicious result, additional procedures would be highly warranted;

- Companion diagnostics – used by physicians to help determine an optimal therapy for a specific patient. An example of this would be HER2+ and Herceptin.

- Recurrence diagnostics are used for patients who had previously been diagnosed with cancer but are currently in remission. In the case of our bladder diagnostic, the test could be used in lieu of a painful, costly cystoscopy to confirm whether the cancer has returned. This test could become part of the follow-up examination of bladder cancer patients; and

Currently we are focused on diagnostics to detect early stage cancer due to the market opportunity associated with these types of diagnostics. Piper Jaffrey estimated that the domestic revenue opportunity for initial diagnosis assays is $15 billion. This is over twice the size of companion/treatment monitoring diagnostics or recurrence diagnostics.

Estimated United States Cancer Diagnostic Market
Revenue by Diagnostic Type

Source: The 2015 Liquid Biopsy Report Piper Jaffrey September 2015
Information on Prognostic is not available

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Oncology Diagnostic Tests Progress to Date

We first announced the development of our confirmatory and screening diagnostics in December 2011 and in conjunction with the Wistar Institute of Anatomy and Biology ("Wistar"), some of whose research in the lung cancer area we have sponsored, we have achieved several key advances since then, including:

- Podium presentation by Wistar of preliminary findings of a proof of concept at American Thoracic Society in May 2015 showing an Area Under the Curve (AUC) of 0.88 for a lung confirmatory mRNA and miRNA classifier
- Supported Wistar's initiation of a clinical study in 2015 collecting blood samples from patients undergoing LDCTs for the detection of lung cancer
- Initiated a first and second clinical study collecting urine samples from patients undergoing cystoscopies to support development of confirmatory and recurrence diagnostics for bladder cancer
- Presented preliminary findings at American Association for Cancer Research in April 2015 showing an AUC of 0.91 for our bladder cancer confirmatory and recurrence diagnostic
- Developed a preliminary classifier diagnostic for breast cancer based on a number of mRNA biomarkers
- Filed several patent applications in the United States and worldwide with claims covering use of various cancer markers in the diagnosis and/or prognosis of various cancers
- Podium presentation by Wistar of a larger proof of concept for a lung confirmatory diagnostic (610 samples) at the Chest conference in October 2016 showing an AUC of 0.82 and sensitivity of 90% and specificity of 62%.
- Poster presentation at San Antonio Breast Cancer Symposium in December of 2016 of a small proof of concept study for a breast confirmatory diagnostic comprised of protein markers with a classifier producing an AUC of 0.92 and a sensitivity of 90% and specificity of 76%

The AUC of a test referenced above is sometimes known as a ROC score and is a measure that combines sensitivity and specificity to express the test's total accuracy, with 1.0 being perfect accuracy and 0.50 being a random result. Sensitivity and specificity are statistical measures of test performance, with sensitivity measuring the percentage of malignant nodules that are identified correctly by the test and specificity measuring the percentage of benign nodules correctly identified.

The Development Pathway

Our liquid biopsy diagnostic tests for cancer will, in general, each go through four stages of development prior to commercialization: 1) Research, 2) Assay development, 3) R&D validation studies, and 4) Clinical validation. The following graph illustrates the development pathway. Although the pathway diagram shows the development process as linear, in practice certain stages of the process may be conducted concurrently rather than sequentially or portions of certain stages may overlap. This general development flow may be customized for each specific product, depending on the circumstances and requirements for that individual test system. A fifth stage, Clinical Utility Studies will also be conducted after commencement of the marketing of a diagnostic test.

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Diagnostic Development Stages

1) Research: The first stage of the development of a CLIA LDT is the research stage. In the research stage of a molecular diagnostic, biological markers are analyzed to determine if specific markers are differentially expressed in certain diseases. We are developing blood and urine tests that differentiate malignant patient samples from benign patient samples by looking at differences in the amount of specific analytes expressed in whole blood or urine from cancer patients compared to patients who are cancer free. For our lung and bladder cancer tests the analytes we are looking at are specific mRNA and/or miRNA expressed in whole blood or urine; while for our breast cancer test we are looking at differently expressing proteins. The objective of this phase of the development process is to delineate promising biomarkers, for further development and verification, before proceeding to validation work.

2) Assay Development: The second stage is Assay Development. In this stage the best performing analytes (mRNA, miRNA, or protein biomarkers) are combined with all of the processes needed to create an assay system. The assay system includes the sample collection methods, sample processing and extractions, biomarker assay methods, and the mathematical “algorithm” required to provide a clinical test result for a sample. The optimal combination and weighting of biomarkers in an algorithm to be used in the final diagnostic are determined through bioinformatics which may be combined with machine learning software strategies that also reflect the biomarker contributions to and reliability within the algorithm. The end result of assay development is an assay system, including a “defined” algorithm, the performance of which has been verified on clinical samples from the targeted ‘intended use’ population. The test system, including the algorithm, can be further optimized during the R&D Validation phase.

3) R&D Validation: The third stage is R&D Validation. There are three areas of studies that are undertaken during R&D Validation. These studies are carried out in our R&D laboratories.

Assay System Reproducibility: During Assay System Reproducibility various critical aspects of diagnostic laboratory procedures are studied and tested to assure that the laboratory can produce consistent, reliable results. Multiple lots of reagents used in the laboratory are tested to determine whether lot to lot differences lead to differences in test results. Procedures for the collection of blood or urine samples from patients, the handling and storage of those samples, and the manner in which the samples are shipped to OncoCyte’s diagnostic testing laboratory, are studied to assure that acceptable procedures are followed and that any variations in the procedures that can occur do not affect the diagnostic test results. Samples are studied for the stability of the biomarkers when the samples are subjected to various conditions that could be encountered throughout the total process of handling and shipping the samples, in order to define the conditions under which the clinical results for the sample will not change, at which point the results will change and lead to a different and erroneous result being reported by the lab.

Algorithm Optimization and Lock: The Algorithm Optimization work that leads to an algorithm lock is usually customized to the needs of the specific product. In the case of the lung cancer test, we are employing a statistical method referred to as cross-validation where the algorithm is optimized on a subset of the clinical samples and then tested on the remaining untested samples. This process of optimizing the algorithm on a subset of samples and then testing on the remaining samples is repeated multiple times. Cross-validation is one of the methods for verifying the algorithm performance that leads to a ‘lock’ on the algorithm.

4) Analytical Validation Studies. The last area of study in R&D Validation is Analytical Validation. The studies required for Analytical Validation have been established in the CLSI (Clinical Lab Standards Institute) Guidelines. These guidelines cover the testing for such matters as limits of quantitation, precision, reproducibility, and interfering substances. When completed, these Analytical Validation studies establish the performance characteristics of the assay system for subsequent clinical validation in the CLIA laboratory.

Clinical Validation: The fourth stage is Clinical Validation. This stage has two distinct sets of studies within it, that are carried out in our CLIA laboratory.

CLIA Lab Validation: In the CLIA Lab Validation Study, the CLIA lab will assay approximately 100 samples previously tested during the R&D Validation stage. This study is to demonstrate that the full assay system utilized in the CLIA lab, run by CLIA staff and on certified instrumentation, provides the same results on clinical samples as those obtained in the R&D lab.

CLIA Lab Clinical Validation. The second kind of study performed in Clinical Validation is the CLIA Lab Clinical Validation. In this study, in general, additional new clinical samples will be collected and sent blinded to the CLIA lab. The CLIA lab will perform assays on these blinded samples and the performance of the full Assay system will be assessed against clinical diagnosis. In the specific case of the lung cancer test, we will perform Clinical Validation on two sets of samples. The first CLIA laboratory Clinical Validation study will test approximately 300 samples. The second study will test approximately 200 additional samples. The performance of the lung cancer test will be compared to clinically confirmed results.

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5) **Clinical Utility:** The final phase of the diagnostic pathway occurs after the diagnostic test has been launched and consists of carrying out one or more Clinical Utility Studies. These studies are important for obtaining coverage and reimbursement by payers such as Medicare, Medicaid, third party commercial insurers, health maintenance organizations ("HMOs"), and large corporations that self-insure. Clinical Utility Studies analyze the healthcare economics associated with a diagnostic test, and in particular whether the test results in overall patient benefits and decreased expenditures for the healthcare system. These studies track the progress of patients who have had the diagnostic test administered; where the diagnostic test has ruled out the possibility of a disease, downstream procedures are tracked to see if the physician's treatment decisions and behavior have changed as a result of having the test result available. The results of this phase may be published in peer review journals and are generally compiled in dossiers to share with managed care groups, including both public and commercial payers. Obtaining positive results that meet endpoints for cost savings or improved outcomes in Clinical Utility Studies is very important in obtaining positive coverage and reimbursement decisions by payers. For example, in our first product candidate - the lung confirmatory diagnostic – the Clinical Utility Study would include patients who have received a suspicious finding in LDCT screening and who then would be tested with our diagnostic. During our post marketing Clinical Utility Studies, we will be tracking patients with a benign result to see if any unnecessary downstream procedures (bronchoscopy or surgical biopsy) are still performed. In other words, we will track whether our diagnostic test reduces unnecessary procedures and decreases the overall cost of diagnosing lung cancer, or whether it is used in addition to downstream procedures, and thereby increases overall costs.

Our lung cancer diagnostic test is in the R&D Validation stage and we anticipate that it will move into Clinical Validation in mid-2017 but there can be no assurance that the development of that diagnostic test will advance in that time frame. Our breast and bladder cancer tests are in the Assay Development stage.

OncoCyte Product Pipeline

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Lung Cancer Diagnostic Test

Current Standard of Care

The current standard of care for diagnosing lung cancer in high risk patients is LDCT scanning. The United States Preventive Services Task force ("USPSTF") guidelines recommend annual LDCTs for patients at high risk for lung cancer. The USPSTF was created in 1984 as an independent, volunteer panel of national experts in prevention and evidence-based medicine. The USPSTF works to improve the health of all Americans by making evidence-based recommendations about clinical preventive services such as screenings, counseling services, and preventive medications.

LDCT Lung Cancer Screening Framework

The guidelines, released in December of 2013, recommend annual LDCT scans for all Americans aged 55 to 80 years old who have a 30 pack-year smoking history and currently smoke or have quit within the past 15 years. A 30 pack-year smoking history is defined as the number of cigarette packs smoked per day times the number of years smoked. A 30 pack-year patient would include the following types of patients:

·Person who has smoked a pack a day (20 cigarettes) for 30 years;

·Person who has smoked 15 cigarettes a day for 40 years; and/or

·Person who has smoked 40 cigarettes a day for 15 years.

These guidelines were driven by a need to improve the standard of care for diagnosing lung cancer. Currently, the survival rate for lung cancer is very low – only 17% of people are still alive five years after a lung cancer diagnosis. These low survival rates result in one of the highest mortality rates for lung cancer, which was projected to kill 158,080 Americans in 2016.

5 Year Survival Rates by Indication
1975 to 2007

Moreover, the survival rate, unlike many other types of cancer, has not increased significantly in the last 30 years. The low probability of surviving lung cancer is significantly affected by the late diagnosis – with more than half of all patients diagnosed after the point that the cancer has spread. USPSTF guidelines were developed to increase the probability of detecting lung cancer in earlier stages, which can significantly improve the survival rates.

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However, the earlier detection of lung cancer will not come without risks. LDCTs are highly sensitive imaging procedures and they result in many false positives. Clinical studies (National Lung Study Trial) have shown initially that 26% of LDCTs are indeterminate of which 96% are shown to be false positives. This results in patients being referred for risky downstream procedures including bronchoscopies, needle biopsies and surgery. These invasive procedures have been shown to result in morbidity and mortality including:

·0.5 to 1% mortality and

·4-20% major complications.

Source: Evaluation of Individuals with Pulmonary Nodules: When is it Lung Cancer? Chest 2013 May: 143 (Suppl):e83-e120.

In order to give clinicians more guidance in managing lung nodules, the American College of Radiology developed the Lung CT Screening Reporting and Data System (Lung-RADS). Lung-RADS was developed to be a quality assurance tool designed to: standardize lung cancer screening reporting and management recommendations; reduce confusion in lung cancer screening interpretation; and facilitate outcome monitoring.

Generally speaking, Lung-RADS divides nodules for clinical management into three categories. For patients with nodules less than 5 mm, no follow-up procedures are necessary; while patients with nodules greater than 5 mm have follow-up procedures . In the case of nodules that are 5 to 8 mm, watchful waiting or serial imaging is recommended. Watchful waiting is the process where an individual is monitored through a series of follow-up scans to see if a nodule grows over time. A patient can be brought back quarterly or semi- annually to monitor if the nodule is growing. Typically, when a nodule has not grown for one to two years, the nodule is considered to be benign. Patients in the third category have nodules over 8 mms and are often recommended for more invasive procedures, such as bronchoscopic biopsy, needle biopsy, open biopsy or video assisted thoracoscopic surgery.

LungRADs Guidelines

Market for Lung Cancer Diagnostic Tests

Lung cancer is a primary cause of cancer-related death, in part because there is no effective diagnostic test to screen patients for lung cancer at an early stage. USPSTF guidelines, which recommend LDCT scans for patients at high risk for lung cancer, may impact up to 10 million Americans who fit the criteria of 30 pack-year smokers. Research has shown that although nodule size is a strong predictor of malignancy, it is not always accurate. Even the largest nodules, those that are greater than three centimeters, have a low malignancy rate of only 41%.

Overall, nodules that are typically sent to biopsy have a malignancy of between 1.7% (for nodules 7 to 10 mm) to 41.3% (for nodules greater than 30 mm). In other words, for every cancer that is found in a biopsy, there are 59% to 98% that are benign. In the case of 7-10 mm nodule, only two out of every hundred biopsies result in a malignancy. This would suggest that a molecular diagnostic that could help clinicians triage patients with intermediate size nodules (8 mm to 30 mm) could significantly reduce the 400,000 biopsies that are projected based on the USPSTF guidelines.

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Nodule Size by Prevalence

We will initially focus on patients with indeterminate diagnoses of larger nodules over 8 millimeters, which is shown as “Initial Focus” in the graph below. These nodules are most likely to be sent for downstream biopsies. This potential market is estimated to include between 400,000 to 600,000 patients annually based on the estimates of patients eligible for USPSTF guidelines (7 to 10 million based on USPSTF and NCI estimates) as well as the approximately 5 million patients with incidentally detected nodules (Gould MK, et al. Aj J Resp Criti Care Med 2015 Nov). We intend to expand the use of our lung cancer diagnostic into smaller nodules shown as “Expanded Use” in the graph below, which targets patients with smaller nodules, who currently are put into a wait and hold pattern and can be scheduled for repeated LDCTs, risking the increase radiation exposure and incurring incremental costs to determine whether the nodule is growing. This will increase the potential patient population to approximately 1.4 million patients. Finally, we may pursue work on a diagnostic that could be used as a screening diagnostic and potentially replace LDCTs for the 7-10 million patients who meet the USPSTF guidelines for high risk, which is represented as the overall lung nodule market in the following graph.

Market Opportunity for Lung Diagnostics

TAM Numbers based on company estimates and secondary data: 7-10 Million screening patients (USPSTF, NCI); 4.9 Million patients with incidental nodules (Gould MK, et al. Am J Respir Crit Care Med 2015 Nov 15; 192 (10):1208-1214).

Clinical Trials

We collaborated with Wistar to develop one of the components of the confirmatory lung cancer diagnostic test in a large, multi-site clinical study. This collaboration involved a clinical study with over 2,000 blood samples obtained from patients with a high risk profile for development of lung cancer, which led to the discovery of biomarkers that differentially express in lung cancer patients. We started enrolling patients in our own clinical trials to provide the data needed to develop the algorithm to combine with the biomarkers and to take the test through analytical and clinical validation. As of the end of January 2017, our clinical trial was being conducted at 36 sites throughout the US.

Large clinical trials are needed to produce patient subsamples that ensure the development of a highly reliable, accurate diagnostic test. In the case of the lung cancer trials, samples are being collected from patients who are at risk for lung cancer, based on having positive or suspicious results from LDCT screening, and who have undergone biopsies to determine the pathology results or who have undergone a series of imaging procedures (LDCT or Petscans) to determine if the nodule is continuing to grow. Additionally, we began collecting samples from patients who used alternative screening procedures such as chest x-rays and who were referred for biopsies.

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Wistar investigators and OncoCyte are currently assessing gene expression patterns in blood cells of patients with imaging detected nodules to differentiate malignant lung nodules from patients with non-malignant lung nodules. Preliminary analysis of patient data from this study was completed during the first quarter of 2015 and preliminary findings from the research showed a sensitivity of 76% and a specificity of 88%. Sensitivity refers to the probability of detecting the presence of the disease accurately; while specificity refers to the probability of accurately predicting not having the disease. Data concerning the OncoCyte/Wistar preliminary lung assay performance with initial biomarkers and classifiers was presented at the American Thoracic Society ("ATS") in May of 2015. The OncoCyte/Wistar preliminary lung assay had a false positive rate of only 12%. In comparison, National Lung Screening Test results reported in the New England Journal of Medicine (August 2011) showed that LDCTs have a very high false positive rate of approximately 96%. The study presented at ATS included both nodules and non-nodules and is the first proof of concept for both our confirmatory and screening lung cancer diagnostic.

Wistar 2015 ATS Presentation
Wistar 2016 Chest Presentation

In October of 2016, Wistar researcher Dr. Louise Showe presented a larger proof of concept study at the Chest annual meeting, where she validated the results of the ATS study with comparable findings. In this larger analysis of 610 patients, Dr. Showe found that the biomarkers alone had an AUC or ROC score of 0.82, resulting in a sensitivity of 90% and a specificity of 62%. These results suggest that a diagnostic comprises of biomarkers and a classifier could help clinicians manage the intermediate size nodules in way that would both improve health outcomes by potentially avoiding morbidity and mortality associated with lung biopsies as well as decreasing the overall costs of lung cancer detection.

To provide independent validation of Wistar's work, we elected to develop our own assay system and algorithm using the biomarkers identified by Dr. Showe at Wistar. We have collected our own clinical samples from 300 patients over 30 sites nationwide. Our study is designed to provide a set of samples that is geographically diverse, from different types of care centers, and that represents a cross-section of the high-risk patient population with nodules. The patients selected for sample collection were believed to have lung nodules of 5 to 30 millimeters in size, which is the size range of nodules in patients for which the lung cancer test system is intended. In performing our analysis of these study samples, we are working closely with the supplier of our analytic platform to optimize reagent and system parameters and metrics to ensure consistent, reliable results from the equipment and reagents we are using to analyze the patient blood samples. We anticipate that we will have the results of our Clinical Validation study at the end of the first quarter of 2017. If successful in this analysis, we will have completed the Assay System Reproducibility and Algorithm Lock phases of R&D Validation. Assuming a successful result, we will immediately complete R&D Validation by carrying out the Analytical Validation and thereafter the Clinical Validation. If we are successful in our 300 sample study, we believe that we will be on track for a commercial launch of the diagnostic test during the second half of 2017, but there can be no assurance that the development of the diagnostic test will be successful or advance in the that time frame.

Breast Cancer Diagnostic Tests

Current Standard of Care

The early detection of cancer is associated with improved outcomes for patients. Mammography has been widely used since the 1970s for breast cancer screening in asymptomatic women; in 2016, over 39 million screening mammograms were performed in the US alone. Current US National Cancer Institute ("NCI") guidelines recommend screening mammograms every one to two years in women 40 years and older, while the American Cancer Society and the National Comprehensive Cancer Network both recommend screening mammography every year starting at age 40. However, in November of 2009, USPSTF revised their screening recommendations increasing the age to 50 and

length of time between screenings from annual to biennial. This was partially driven by the concerns around false positives. Approximately 10% of women are recalled from screening mammography for further testing and approximately 95% of those women's test results end up as false positives. Over the course of 10 years of screening, one out of every two women will experience a false positive with 7% to 17% of those women having unnecessary biopsies. (Rosenberg RD et al. Radiology 2006. Elmore JG et al. N Engl J Med 1998, Hubbard RA et al. Ann Intern Med 2011, Rosenberg RD et al. Radiology 1998, Kerlikowske K et al. JAMA 1996, Porter PL et al. J Natl Cancer Inst 1999)

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At the same time, mammography screening in women aged 40 to 74 has been associated with the relative reduction in breast cancer mortality of 15% to 20%. However, the NCI estimates that approximately 20% of all breast cancers are not detected by mammography during screening. In the case of women with dense breast tissue, mammography has been shown to have poor sensitivity with only 62-69% of all cancers detected (Carney et al 2003, Pisano et al 2006) This has resulted in 27 state legislatures dictating that radiologists notify women about the difficulties of detecting breast cancer in dense breast tissue and that supplemental screening may be appropriate. These false negatives or missed diagnoses, together with the false positives or over diagnoses, indicate a strong unmet need for a breast cancer screening test with superior specificity and sensitivity when compared to standard screening mammography.

Additionally, guidelines recommend MRI screening for approximately 6 million women who either have a family history, a BRCA gene mutation or dense breast tissue, since mammograms have been shown to miss cases of cancer in patients that meet these profiles.

Breast Cancer Screening Protocol

OncoCyte is developing a confirmatory diagnostic test that could be used with women who have an indeterminate mammogram result (BI-RADS 3 or 4). In the case of a mammogram BI-RADS 3 score, repeat imaging is recommended, which means that women may have to schedule another mammogram or they may be referred to a more costly MRI procedure. In the case of a mammogram BI-RADS 4 score, women are often referred for a biopsy. Our breast confirmatory diagnostic could be incorporated into breast screening protocols to confirm whether women with BI-RADS 3 or 4 scores need to undergo additional costly imaging or an invasive biopsy.

Market Opportunity

Each year approximately 5% of women have mammograms that are suspicious and many of these women are sent on to biopsies (Geller et al Radiology 222:2 2002). Currently it is estimated that about 16% or 250,000 of these biopsies will be cancerous. This is the focus of our initial research for our breast cancer confirmatory diagnostic as shown in the following graph. We are planning to expand our research efforts to include the second intended use – women who meet the guidelines for MRIs. There are over 6 million women in the U.S. for whom the guidelines recommend both a mammogram and a MRI yearly.

We plan to expand the use of our diagnostic in the future to meet the needs for a better breast cancer screening diagnostic, which could impact up to 38 million women each year. Research over the last 25 years has shown that large numbers of women are having unnecessary biopsies resulting in estimates of $4 billion a year being spent on false positives (Health Affairs, 34, no.4 (2015):576-583).

Market Opportunity for Breast Cancer Diagnostic Tests

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Breast Cancer Diagnostic Clinical Trials

We completed a strong proof of concept for our breast confirmatory test and presented this data at the San Antonio Breast Cancer Symposium (SABCS) in December of 2016. Our study looked at serum from 100 women who had a mammogram with a result of BIRADs 3 or 4. These samples were collected over approximately two years during 2014 and 2016 and by March of 2016, we had collected over 900 patient blood samples. The 100 women whose samples were used in the analysis were all sent for biopsies and half them had a pathology confirmed benign and half of them had a pathology confirmed malignant. The analysis looked at proteins that were differentially expressing in women with malignances from a large screen of 1,310 proteins.

The results of this analysis were quite promising with a 15 marker model producing a sensitivity of 90% and a specificity of 76%. The analysis was a strong proof of concept that a non-invasive blood test could help differentiate women with indeterminate mammograms into two groups – those needing to be biopsied and those for whom the finding was highly likely to be benign.

We are continuing development of a breast cancer confirmatory diagnostic by conducting a larger study that we expect will analyze blood samples from approximately 300 patients with benign or malignant nodules. If this analysis is successful and we are able to reproduce the results presented at SABCS, we will lock down the assay and start the R&D validation.

Bladder Cancer Diagnostic Tests

Current Standard of Care

The current standard of care for bladder cancer diagnosis is cytology and cystoscopies. Urine cytology is a test to look for abnormal cells in a patient’s urine. Urine cytology is used along with other tests and procedures to diagnose urinary tract cancers. Cystoscopy is a procedure that allows a doctor to examine the lining of the bladder and the urethra, tube that carries urine out of the body. A hollow tube called a cystoscope, equipped with a lens, is inserted into the patient’s urethra and slowly advanced into the bladder. Increasingly over the years, cystoscopies have been used in conjunction with cytology which has resulted in increasing costs for the detection of bladder cancer.

Current Bladder Diagnostic Protocol

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Market Opportunity

Bladder cancer has the highest lifetime treatment costs per patient of all cancers. The high recurrence rate and ongoing invasive monitoring requirement are the key contributors to the economic and human toll of this disease.

Urothelial carcinoma constitutes more than 90% of bladder cancers in the Americas, Europe and Asia. Although most patients with bladder cancer can be treated with organ-sparing chemotherapy, UC has a relapse rate of nearly 70% and can progress to invasive, metastatic, and lethal disease. The regular surveillance and treatment of recurrent disease from the time of diagnosis for the remainder of a patient's life makes urothelial Carcinoma the most costly malignancy on a per patient basis. The problem is amplified because the two standard methods for surveillance - microscopic assessment of urinary cytology specimens and bladder cystoscopy – which possess significant limitations with respect to both performance and cost. Although urine cytology does have a very high positive predictive value and low false positive rate, it has a low negative predictive value and a high indeterminate rate. Patients who have indeterminate urine cytology results commonly undergo cystoscopy, which is painful, time consuming, costly, and unnecessary in many cases since a neoplasm is often not present. In urothelial carcinoma, as in virtually all other cancers, earlier and more accurate diagnosis, including diagnosis of disease recurrence, is generally associated with better outcomes and lower cost.

Bladder Diagnostic Market Opportunity

TAM numbers based on company estimates and secondary data

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Overall markets for bladder cancer diagnostics are large and growing. Based on National Cancer Institute statistics released in 2012, it was estimated that in 2013 over 72,000 new cases of bladder cancer would occur in the United States and a total of over 550,000 men and women alive would have a history of bladder cancer and be subject to recurrence surveillance testing using cystoscopy or urine cytology. Additionally, another 3 million patients present yearly with hematuria (blood in urine), an early symptom of bladder cancer and 500,000 patients have indeterminate cytology findings. These three patient profiles: indeterminate cytology, hematuria and surveillance, could result in a potential market opportunity of approximately 4.5 million tests yearly.

Sending urine specimens to us for analysis using our diagnostic tests instead of performing a cystoscopy procedure would be a significant departure from the current standard of care in the diagnosis of bladder cancer. Urologists may be reluctant or unwilling to change their practices and utilize our diagnostic test for bladder cancer even if our test is proven to have a high rate of accuracy in detecting the presence or absence of cancer.

The potential resistance of urologists to adopt the use of our bladder cancer diagnostic test means that marketing that test could require a substantial effort by a sales force. Due to this concern and our limited financial and marketing resources, we may seek to enter into an agreement with a larger company that has greater marketing resources for the marketing of our bladder cancer test. We may license out both completion of development and marketing to another company, retaining rights to receive a royalty on sales and possibly some sales related milestone payments, or we may complete the development of the test and seek to co-market the test with another company in an arrangement that might provide for a sharing of marketing costs and revenues. There is no assurance that we will be successful in entering into a licensing or co-marketing arrangement or that a licensee or co-marketing partner will succeed in marketing our bladder cancer diagnostic test. If we enter into a license or co-marketing agreement, our revenues from the sale of our bladder cancer diagnostic test may be substantially less than the amount of revenues and gross profits that we might receive if we were to market that diagnostic test ourselves.

Bladder Cancer Diagnostic Test Clinical Trials

As part of our clinical development of a urine-based bladder cancer diagnostic test, we initiated a clinical trial in January 2014 that has been expanded to a multi-site trial. The trial will involve up to 1,400 patient samples obtained from at least nine large urology clinics located throughout the United States. As of March 2016, we had approximately 1,275 samples in house. The clinical trial is designed to expand the potential use of our bladder cancer test beyond pathology laboratories and into urologic practices at the point of cystoscopy. The goal of the current clinical trial is to compare the performance of our bladder cancer markers to the performance of cystoscopy. Investigators in the trial are collecting urine samples from patients undergoing cystoscopy for the diagnosis of either primary or recurrent bladder cancer. Cystoscopy and biopsy results will be compared with the results of our proprietary diagnostic test panel in determining the overall performance of our classifier and markers.

In May of 2015, we presented preliminary findings of our bladder research at the American Association of Cancer Research. Preliminary findings showed a sensitivity of 90% and a specificity of 83%. Sensitivity is the probability of detecting the presence of the disease accurately. A sensitivity of 90% means that 9 out of 10 cancers were detected. Specificity is the probability of accurately predicting not having the disease.

We have decided to pursue a co-development partner for our bladder cancer test.

Future Diagnostic Development Milestones

Over the next two years, our goal is to achieve the following milestones relating to the development and commercialization of our cancer diagnostic tests:

·Out-licensing or co-marketing partnership for our bladder cancer confirmatory and recurrence diagnostic;

- Locking down the assay for our lung cancer confirmatory diagnostic;
- Analytical validation and clinical validation of our lung cancer confirmatory assay;
- Establish a CLIA laboratory and obtain a certificate of registration, a certificate of compliance and inspection for all 50 states;
- Launch of a confirmatory diagnostic test for lung cancer;
- Locked down assay for a breast cancer confirmatory diagnostic for women with suspicious mammograms;
- Completion of clinical utility studies for lung cancer confirmatory diagnostic;

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- Submit dossier to CMS for Medicare coverage for our lung cancer confirmatory diagnostic;

- Completion of a prospective patient study for analytical validation and clinical validation of our breast cancer diagnostic;

- Analytical validation and clinical validation of our breast cancer confirmatory assay;

- Proof of concept for a pipeline product (fourth indication) with high clinical unmet need.

Achieving the milestones will require expanding our Commercial team to include sales, market access, customer support and medical affairs. This increased staffing will be used to seed the market for our lung cancer diagnostic, gain reimbursement coverage, and support the ordering of our diagnostic.

Technology for Diagnostic Tests

In our liquid biopsy tests for lung, breast and bladder cancer, we are using the same general strategy for the identification of mRNA, miRNA and protein biomarkers and are developing a gene expression classifier to interpret the differential marker expression. Our tests are being developed to yield a highly accurate benign call to allow clinicians to triage patients for follow-up procedures. Ultimately our research may rely on only one type of biomarker in a specific indication. In the case of lung cancer, our test will be developed on mRNA biomarkers only. In the case of breast cancer, our study has evolved from the use of RNA markers and monoclonal antibodies directed to proteins to proteins only.

In the case of our lung cancer assay, blood samples are collected by venipuncture into tubes and total RNA is isolated. mRNA biomarkers were identified using microarray equipment. The best performing mRNA biomarkers will be transferred to the commercial platform we will use in our CLIA laboratory. Differentially expressed miRNAs will be identified by screening the human V3 miRNA panel or alternative RNA detection methods. The optimal combination and final panel of mRNA and miRNA biomarkers together with potential protein-based assays will be determined using bioinformatics and machine learning strategies. The optimal classifier will be developed that yields the best discrimination between malignant and benign. The performance of the final biomarker panel and classifier will be tested on an independent set of samples to determine performance characteristics.

For bladder cancer, we are developing a urine test for use in recurrence screening and hematuria. The bladder cancer diagnostic is based on differential mRNA expression in urine samples. mRNA biomarkers were identified using microarray and top biomarkers were transferred to the commercial platform. A streamlined assay was developed that uses crude urine sediment lysates rather than purified RNA, eliminating the need for RNA isolation and amplification. The optimal classifier will be developed that yields the best discrimination between malignant and benign. The performance of the final biomarker panel and classifier will be tested on an independent set of samples to determine performance characteristics.

Biomarkers are important to the diagnosis of cancer in that their presence or absence in a specific patient sample drives the sensitivity and specificity scores of a molecular diagnostic. For example, if a specific mRNA is only seen expressed in patients with cancer, it can be used to help make a malignant call on that sample. The use of biomarkers with a classifier can help ensure that the sensitivity score, which is a measure of correcting identifying the disease is sufficiently high to reduce false negative, ensuring that patients with the disease are correctly diagnosed. At the same time, biomarkers can be used to hone the specificity measure, which is a measure of correctly identifying patients without the disease, which reduces the number of patients who are unnecessarily referred to biopsy.

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Licensed Technology from Wistar

We have entered into a License Agreement with Wistar that entitles us to use certain patents, know-how and data belonging to Wistar, including technology and data developed by Wistar at our expenses under a Sponsored Research Agreement for work completed during 2016.

Licenses Granted

Under the License Agreement, we have obtained an exclusive, worldwide license under certain patents, and under certain know-how and data ("Technical Information") belonging to Wistar, for use in the field of molecular diagnostics for lung cancer, including, but not limited to confirmatory, companion and recurrence diagnostics for any type of lung cancer with detection through whole blood, fractionated blood, plasma, serum and/or other biological samples (the "Licensed Field").

We have the right to grant sublicenses of the licensed patents and Technical Information. The sub-licensee will be subject to Wistar's approval, which will not be unreasonably withheld, if we are not selling a "Licensed Product." As used in the License Agreement, a Licensed Product means any product that cannot be made, used, or sold, or any service, process or method that cannot be performed or provided, without infringing at least one pending or issued valid claim under the licensed patents in a particular country, or that incorporates or is made, identified, developed, optimized, characterized, selected, derived or determined to have utility, in whole or in part, by the use or modification of any licensed patent or any technology or invention covered thereby, any licensed Technical Information, or any other Licensed Product.

Royalties, License Fees and Other Payment Obligations

We have paid Wistar an initial license fee and will pay Wistar royalties on net sales, as defined in the License Agreement, of Licensed Products. The royalty rates will range from 3% to 5% depending upon the amount of our cumulative net sales of Licensed Products. If we are required to pay to royalties to a third party in order to manufacture or sell a Licensed Product in a particular country, the amount of royalties that we must pay Wistar on net sales of the Licensed Product will be reduced by the amount of royalties that we must pay to the third party, but subject to a maximum reduction of 50%. Our obligation to pay royalties to Wistar will terminate on a Licensed Product by-Licensed Product and country-by-country basis until the later of (i) the date a valid claim of a licensed patent covering the Licensed Product no longer exists, or (ii) the tenth (10th) anniversary of the first commercial sale of the Licensed Product in each country.

We will pay Wistar a minimum annual royalty during each subsequent year, which in each case will be credited against total royalties due on net sales of Licensed Products during the year in which the minimum royalty is paid. We will also be obligated to pay Wistar an annual license maintenance fee each year unless we initiate sales of at least one Licensed Product by January 1, 2018.

In addition to royalties on net sales, if we grant any sublicense to the licensed patents or Technical Information, we will pay Wistar a portion of any non-royalty sublicensing income that we may receive from the sub-licensee. Non-royalty sublicensing income will include any consideration we receive from a sub-licensee for granting the sublicense, but excluding royalties on net sales of Licensed Products, the fair market value of any equity or debt securities we may sell to a sub-licensee, and any payments we may receive from a sub-licensee for research of a Licensed Product that we may conduct.

We also will pay Wistar (a) milestone payments upon the occurrence of certain milestone events in the development and commercialization of a Licensed Product, and (b) all past or ongoing costs incurred or to be incurred by Wistar, including government fees and attorneys' fees, in the course of prosecuting the licensed patents.

Other Obligations

We have agreed to use commercially reasonable diligent efforts, directly or through sub-licensees, to develop and commercialize Licensed Products. We will provide Wistar with written plans for the development and commercialization of Licensed Products and Wistar has the right to raise reasonable objections to our plans. We will also provide Wistar with annual reports on our progress in developing, evaluating, testing, and commercializing Licensed Products. We have agreed that we or a sub-licensee will commence commercial sale of a Licensed Product by a specified date. If sales of a Licensed Product do not commence by the specified date, we may purchase up to three one-year extensions of the deadline by paying Wistar a designated fee for the applicable extension.

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We have agreed to indemnify Wistar and its trustees, managers, officers, agents, employees, faculty, affiliated investigators, personnel and staff (the "Indemnified Parties"), from and against any and all liability, loss, damage, action, claim or expense (including attorney's fees) suffered or incurred by the Indemnified Parties due to claims which result from or arise out of (a) the License Agreement and the license granted to us, and any sublicense granted pursuant to the License Agreement, (b) the development, use, manufacture, promotion, sale or other disposition of the licensed patents, licensed Technical Information or any Licensed Products, (c) the breach of any our representations, warranties, or covenants in the License Agreement, or a breach of a sublicense by a sub-licensee, or (d) the successful enforcement by an Indemnified Party of its indemnification rights under the License Agreement. This indemnification obligation shall apply to liabilities resulting from: (i) any product liability or other claim of any kind related to the use of a Licensed Product; (ii) any claim that the licensed patents or the design, composition, manufacture, use, sale or other disposition of any Licensed Product infringes or violates any patent, copyright, trademark or other intellectual property rights of any third party; or (iii) clinical trials or studies conducted by or on behalf of us or any sub-licensee relating to the Licensed Products. Notwithstanding the foregoing, we will not be obligated to indemnify and hold harmless the Indemnified Parties from and against any liabilities that result from or arise out of an Indemnified Party's gross negligence or willful misconduct.

Termination of the License Agreement

Wistar has the right to terminate the License Agreement, subject to certain notice and cure periods and force majeure delays in certain cases, if any of the following occur: (a) we fail to pay any amount payable to Wistar; (b) we materially breach any covenant or agreement or any continuing representation or warranty contained in the License Agreement; (c) we become subject to certain bankruptcy or insolvency events, (d) we dissolve or cease operations, (e) we or any of our affiliates or sub-licensees or affiliates of any our sub-licensees challenges the validity, patentability, scope, construction, enforceability, non-infringement, or Wistar's ownership of any issued patent comprising the licensed patents, or assists any third party in any such challenge; or (f) we fail to fulfill our product development and commercialization diligence obligations and related performance milestones.

We have the right to terminate the License Agreement, subject to a notice and cure period, if Wistar materially breaches the License Agreement. At any time after the second anniversary date of the License Agreement we may terminate the License Agreement, with or without cause, upon the passage of a specified period of time after giving Wistar written notice of termination.

Wistar's Retained Rights to Certain Proposed Products

Wistar has reserved the right to (i) make, use, practice and further develop the licensed patents and Technical Information for educational, research, and other internal purposes; (ii) grant to any academic, government, research or non-profit institution or organization the right to make, use and practice the licensed patents or Technical Information for non-commercial research and educational purposes; and (iii) grant licenses under the Licensed Patents or Technical Information to any party for any field, product, service or territory other than the Licensed Products in the Licensed Field.

In addition, if Wistar determines to develop or have developed an actual or potential Licensed Product that is for an application, product, sub-field or indication in the Licensed Field, but for which Wistar reasonably believes a Licensed Product is not being actively developed or commercialized by us or by our affiliates or sub-licensees, Wistar may give us notice of the proposed product. If we timely inform Wistar of our election to develop the proposed product, and if we successfully negotiate a development plan and milestones for the proposed product, we will be entitled to develop the proposed product as a Licensed Product under the License Agreement. If we do not elect to develop the proposed product or do not reach agreement with Wistar for a development plan and milestones for the proposed product, Wistar may exclude the proposed product from our license under the License Agreement and may develop the proposed product itself or grant licenses to third parties under the licensed patents and Technical Information for the

development and commercialization of the proposed product.

Manufacturing

Facilities Required

Under a Shared Facilities and Services Agreement (the "Shared Facilities Agreement") with BioTime, we have use of laboratory and office space at BioTime's facility in Alameda, California. BioTime has leased approximately 30,795 square feet of office and laboratory space in two buildings located in Alameda, and will provide OncoCyte use of space sufficient for a CLIA compliant diagnostic laboratory.

Raw Materials

The processing of our diagnostics will use commercially available reagents that are sourced by a well-known manufacturer of molecular diagnostic analyzers, prep stations and reagents that has been in business for over 12 years. Although we do not believe that we will encounter sourcing issues for these supplies, if an interruption in supply were to occur, we might need to find a different source of supply of both the reagents and the analytic equipment that we will be using in our CLIA laboratory. An interruption in supply of reagents could cause us to suspend or limit laboratory operations, and a change in analytic equipment could require us to re-establish various testing procedures, which also could disrupt our operations.

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Marketing

Following CLIA certification for our laboratory and diagnostic tests, we intend to market our diagnostic tests directly to health care providers working in the areas of lung cancer and in other areas of cancer where we will be developing molecular diagnostics. These health care providers will collect blood samples or send patients to laboratories to have blood or urine samples collected. These samples, also referred to as liquid biopsies, will be sent to our CLIA laboratory in California, either by the health care provider or the laboratory, where the sample will be run through an assay and a gene expression classifier to determine a binary result, either benign or suspicious. That result will be presented to the physician ordering the procedure in a standardized report.

We will ramp up sales and marketing teams over the next two to three years. Over time, we will continue to grow our sales, market access and marketing organizations to increase the awareness and utilization of our diagnostic tests and to prepare for additional diagnostic test launches. The focus of our marketing organization will be to address the benefits of our planned lung cancer confirmatory diagnostic to the three key stakeholders: physician, patients and payers.

We will target three specialty physician groups, who either do the screening for lung cancer or conduct the biopsies or serial imaging downstream procedures. These groups are pulmonologists, radiologists and thoracic surgeons. The focus of our physician marketing efforts will be outreach through:

- medical conferences and symposia, for which the primary conferences are Chest and American Thoracic Society
- speakers bureaus
- peer review journal articles

If our diagnostic advances through development, we plan a major presence this year at the American Thoracic Society international conference in Washington D.C. May 19-24 and at the Chest International Conference in Toronto, Canada October 28 through November 1.

If we are successful in developing our diagnostic, our marketing efforts to patients will be focused on increasing the awareness of lung cancer screening through work with advocacy groups and/or patient outreach. Additionally, we will be developing a patient assistance program to help reduce the financial burden to patients of out of pocket expenses due to lack of insurance coverage, high co-insurance payments or high deductibles.

Our marketing outreach to third party payers such as health insurers will be driven by our “Market Access Team.”

Market Access – Reimbursement

One of the more critical functions in a diagnostic company is market access. We are forming a Market Access Team that will develop and implement our strategy to obtain coverage and reimbursement from public and private payers. For an oncology diagnostic, one of the most critical payers is Medicare or CMS, because oncology is a cancer that presents in older populations. We estimate that for our lung test, that over time, Medicare may cover up to 55% of the patients for whom the test is ordered. We started the Market Access Team in mid-2016 with the lead for the team, who has over 10 years of molecular diagnostics market access and commercial operations experience.

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It generally takes two to three years to obtain Medicare reimbursement coverage, and can take up to another two to three years to obtain other third party reimbursement approvals, for a new LTD and there can be no assurance we will obtain such approvals for any of the cancer diagnostics that we are developing. Until a new cancer diagnostic test is accepted by third party payers for reimbursement, we will have to market the test to physicians on a patient pay basis—in other words the patient will need to pay the full cost of the test. In the absence of reimbursement by a health insurance plan or Medicare, patients who would be candidates for the use of our diagnostic tests may decline to use our tests, and physicians may be reluctant to prescribe our tests, due to the cost of the test to the patients. Because of this patient cost factor, revenues from any new cancer test that we market will experience slow growth until the test is approved for reimbursement in an amount commensurate with the cost to the patient.

Our market access strategy is based on three components: coding, coverage and reimbursement. For product coding we will launch our diagnostic with an unlisted code and seek to get a unique CPT code later. We believe that our lung cancer confirmatory diagnostic will meet the requirements of a Multi Analyte Algorithm Assay (MAAA) in that the diagnostic that we are developing will be comprised of multiple mRNA biomarkers with a gene expression classifier.

The second focus of our reimbursement strategy will be to obtain coverage by both public and commercial payors. We will first focus on receiving a Medicare coverage decision and then focus on obtaining coverage decisions for larger commercial payors, including private health insurance plans. Medicare through the MolDX program has developed clear guidelines for the level of evidence of efficacy required to be obtained through clinical trials. Our strategy is to achieve the highest level of evidence (IIA) by developing clinical protocol designs for both our clinical validation and clinical utility studies that are randomized and prospective. Additionally, our plan is to run two clinical validation studies and between two or three clinical utility studies to meet or surpass the minimum MolDX requirement (IIB). We took the approach of sharing our clinical protocol designs with payors, much like many therapeutic companies share their clinical utility designs with the FDA, for feedback.

We previewed our clinical protocol designs with ten payers that represent over 77 million covered lives late last year and received favorable feedback on the design of our studies, the number of our studies, and the primary and secondary endpoints. From this interaction, we believe that if we are successful in meeting the endpoints of our clinical utility studies, we will receive favorable coverage decisions by some large payers.

Patents and Trade Secrets

We rely primarily on patents and contractual obligations with employees and third parties to protect our proprietary rights. We have sought, and intend to continue to seek, appropriate patent protection for important and strategic components of our proprietary technologies by filing patent applications in the U.S. and certain foreign countries. There can be no assurance that any of our patents will guarantee protection or market exclusivity for our diagnostic tests and diagnostic test candidates. We may also use license agreements both to access technologies developed by other companies and universities and to convey certain intellectual property rights to others. Our financial success will be dependent in part on our ability to obtain commercially valuable patent claims and to protect our intellectual property rights and to operate without infringing upon the proprietary rights of others.

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Our diagnostic patent portfolio includes 13 patent families owned by us with claims directed to compositions of matter and methods useful for detection of breast, bladder, colon, pancreatic, ovarian, and thyroid cancers using specific biomarkers or a panel of specific biomarkers. Patents are pending in various jurisdictions, including the United States, Europe, Australia, Canada, China, Hong Kong, Japan and Republic of Korea, with projected expiration dates ranging from 2032 to 2036. Additionally, we have one issued patent in Australia, with claims directed to a method of detecting bladder cancer; and one accepted patent application in Australia, with claims directed to a method of detecting breast cancer. The issued patent will expire in 2032.

We have also obtained an exclusive license from Wistar to certain pending patent applications in the field of molecular diagnostics for lung cancer. The pending claims are directed to compositions of matter and methods useful for detection of lung cancer using specific biomarkers or a panel of specific biomarkers, with projected expiration dates in 2036. Additionally, we have obtained from Wistar an exclusive option under which we may obtain licenses to additional issued and pending patents in the field of molecular diagnostics for lung cancer. Patents covered by the exclusive option have issued in the United States and Europe and are pending in the United States, Canada and India. Those patents are projected to expire in 2028 - 2030.

In addition to relying on patents, we will rely on trade secrets, know-how, and continuing technological advancement to maintain our competitive position. We have entered into intellectual property, invention, and non-disclosure agreements with our employees, and it is our practice to enter into confidentiality agreements with our consultants. There can be no assurance, however, that these measures will prevent the unauthorized disclosure or use of our trade secrets and know-how, or that others may not independently develop similar trade secrets and know-how or obtain access to our trade secrets, know-how, or proprietary technology.

General Risks Related to Obtaining and Enforcing Patent Protection

Our patents and patent applications are directed to compositions of matter, formulations, methods of use and/or methods of manufacturing. The patent positions of pharmaceutical and biotechnology companies, including ours, are generally uncertain and involve complex legal and factual questions. Our business could be negatively impacted by any of the following:

- The claims of any patents that are issued may not provide meaningful protection, may not provide a basis for commercially viable diagnostic tests or may not provide us with any competitive advantages;
- Our patents may be challenged by third parties;
- Others may have patents that relate to our technology or business that may prevent us from marketing our diagnostic test candidates unless we are able to obtain a license to those patents;
- Patent applications to which we have rights may not result in issued patents; and
- We may not be successful in developing additional proprietary technologies that are patentable.

In addition, others may independently develop similar or alternative technologies, duplicate any of our technologies and, if patents are licensed or issued to us, design around the patented technologies licensed to or developed by us. Moreover, we could incur substantial costs in litigation if we have to defend ourselves in patent lawsuits brought by third parties or if we initiate such lawsuits

The United States Supreme Court’s decisions in Mayo Collaborative Services v. Prometheus Laboratories, Inc. and Association for Molecular Pathology v. Myriad Genetics may limit our ability to obtain patent protection on diagnostic methods that merely recite a correlation between a naturally occurring event and a diagnostic outcome

associated with that event. Our cancer diagnostic tests are based on the presence of certain genetic markers for a variety of cancers. In Mayo Collaborative Services v. Prometheus Laboratories, Inc., the Supreme Court ruled that patent protection is not available for the use of a mathematical correlation of the presence of a well-known naturally occurring metabolite as a means of determining proper drug dosage. The claims in the contested patents that were the subject of that decision were directed to measuring the serum level of a drug metabolite and adjusting the dosing regimen of the drug based on the metabolite level. The Supreme Court said that a patent claim that merely claimed a correlation between the blood levels of a drug metabolite and the best dosage of the drug was not patentable subject matter because it did no more than recite a correlation that occurs in nature.

In Association for Molecular Pathology v. Myriad Genetics, the Supreme Court ruled that the discovery of the precise location and sequence of certain genes, mutations of which can dramatically increase the risk of breast and ovarian cancer, was not patentable. Knowledge of the gene location and sequences was used to determine the genes' typical nucleotide sequence, which, in turn, enabled the development of medical tests useful for detecting mutations in these genes in a particular patient to assess the patient's cancer risk. But the mere discovery of an important and useful gene did not render the genes patentable as a new composition of matter.

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Also, in Ariosa Diagnostics, Inc. v. Sequenom, Inc., the Federal Circuit ruled that a method for detecting a paternally inherited nucleic acid of fetal origin performed on a maternal serum or plasma sample from a pregnant female was not patent eligible subject matter under the framework set forth in Mayo Collaborative Services v. Prometheus Laboratories, Inc. The court examined the elements of the claim to determine whether the claim contained an inventive concept sufficient to transform the claimed naturally occurring phenomenon into a patent eligible application and found that the method steps did not support patentability because they used conventional amplification and detection techniques. Although the claims can be distinguished from the claims at issue in Mayo Collaborative Services v. Prometheus Laboratories, Inc., the court was bound by the language of the Supreme Court decision to hold Sequenom's claims unpatentable.

While the cases discussed above are instructive, the United States Patent and Trademark Office (the "USPTO") has issued interim guidelines in light of the Supreme Court decisions indicating that process claims having a natural principle as a limiting step will be evaluated to determine if the claim includes additional steps that practically apply the natural principle such that the claim amounts to significantly more than the natural principle itself. Because the diagnostic tests that we are developing combine an innovative methodology with newly discovered compositions of matter, we are hopeful that this Supreme Court decision will not preclude the availability of patent protection for our diagnostic tests.

The USPTO has also issued a Subject Matter Eligibility Update to provide further guidance in determining subject matter eligibility. The Subject Matter Eligibility Update includes new Subject Matter Eligibility Examples for the Life Sciences. These examples provide favorable exemplary subject matter eligibility analysis of hypothetical claims covering diagnostic tests and claims drawn from case law. This update from the USPTO does not change our opinion on our ability to obtain meaningful patent protection.

There is a risk that any patent applications that we file and any patents that we hold or later obtain could be challenged by third parties and declared invalid or infringing of third party claims. A patent interference proceeding may be instituted with the USPTO when more than one person files a patent application covering the same technology, or if someone wishes to challenge the validity of an issued patent filed before March 16, 2013. At the completion of the interference proceeding, the USPTO will determine which competing applicant is entitled to the patent, or whether an issued patent is valid. Patent interference proceedings are complex, highly contested legal proceedings, and the USPTO's decision is subject to appeal. This means that if an interference proceeding arises with respect to any of our patent applications, we may experience significant expenses and delay in obtaining a patent, and if the outcome of the proceeding is unfavorable to us, the patent could be issued to a competitor rather than to us. In addition to interference proceedings, the USPTO can reexamine issued patents at the request of a third party seeking to have the patent invalidated. After March 16, 2013 an inter partes review proceeding will allow third parties to challenge the validity of an issued patent where there is a reasonable likelihood of invalidity. This means that patents owned or licensed by us may be subject to re-examination and may be lost if the outcome of the re-examination is unfavorable to us.

Post Grant Review under the America Invents Act makes available opposition-like proceedings in the United States. As with the USPTO interference proceedings, Post Grant Review proceedings will be very expensive to contest and can result in significant delays in obtaining patent protection or can result in a denial of a patent application. Also, a derivation proceeding may be instituted by the USPTO or an inventor alleging that a patent or application was derived from the work of another inventor.

Oppositions to the issuance of patents may be filed under European patent law and the patent laws of certain other countries. As with the USPTO interference proceedings, these foreign proceedings can be very expensive to contest and can result in significant delays in obtaining a patent or can result in a denial of a patent application.

The enforcement of patent rights often requires litigation against third party infringers, and such litigation can be costly to pursue. Even if we succeed in having new patents issued or in defending any challenge to issued patents,

there is no assurance that our patents will be comprehensive enough to provide us with meaningful patent protection against our competitors.

In addition to patents, we rely on trade secrets, know-how, and continuing technological advancement to maintain our competitive position. The molecular diagnostics that we are developing use gene expression classifiers, which are mathematical models that weight the biomarkers to produce a score, that we plan to protect as. The mathematical model will be protected by trade secrets. We have entered into intellectual property, invention, and non-disclosure agreements with our employees, and it is our practice to enter into confidentiality agreements with our consultants. There can be no assurance, however, that these measures will prevent the unauthorized disclosure or use of our trade secrets and know-how, or that others may not independently develop similar trade secrets and know-how or obtain access to our trade secrets, know-how, or proprietary technology.

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Third-Party Payer Reimbursement

Billing, Coverage, and Reimbursement for Diagnostic tests

Revenues from our clinical laboratory testing will be derived from several different sources. Depending on the billing arrangement, the instruction of the ordering physician, and applicable law, parties that may reimburse us for our services include:

- Third-party payers that provide coverage to the patient, such as an insurance company, a managed care organization, or a governmental payer program;
- Physicians or other authorized parties, such as hospitals or independent laboratories, that order the testing service or otherwise refer the testing services to us; or
- Patients in cases where the patient has no insurance, has insurance that partially covers the testing, or owes a co-payment, co-insurance, or deductible amount.

Medicare

We expect that a substantial portion of the patients for whom we may perform diagnostic tests will have Medicare as their primary medical insurance. We cannot assure that, without Medicare reimbursement our planned tests will produce sufficient revenues to enable us to reach profitability and achieve our other commercial objectives.

Clinical diagnostic laboratory tests are generally reimbursed under the Medicare Clinical Laboratory Fee Schedule ("CLFS"), and reimbursement under the Medicare program for the diagnostic tests that we will offer is based on the CLFS.

Medicare payment amounts are established for each Current Procedural Terminology (“CPT”) code. CPT codes are the main data code set used by physicians, hospitals, laboratories and other health care professionals to report separately-payable clinical laboratory services for reimbursement purposes. The CPT coding system is maintained and updated on a quarterly basis by the American Medical Association (“AMA”). Each quarter, new laboratory test codes are added to the fee schedules and corresponding fees are developed in response to a public comment process. We will request a unique CPT code from the AMA for our diagnostic test. Any updates and changes in CPT coding and reimbursement methods could impact our revenues. The introduction of new codes by Centers for Medicare and Medicaid Services (“CMS”) in combination with other actions with regard to pricing could result in (i) lower reimbursements to us than those we may anticipate, or (ii) a reduction in the payments that we may receive for our tests, and could make it more difficult to obtain coverage from Medicare or other payers. There can be no guarantees that Medicare and other payers will establish positive or adequate coverage policies or reimbursement rates.

In addition, under the CLFS, Medicare also sets a cap on the amount that it will pay for any individual test. This cap, usually referred to as the national limitation amount, is set at a percentage of the median of all the contractor fee schedule amounts for each billing code.

Medicare has coverage policies that can be national or regional in scope. Coverage means that the test is approved as a benefit for Medicare beneficiaries. If there is no coverage, neither we nor any other party, such as a reference laboratory, may receive reimbursement from Medicare for the service.

Legislative and Regulatory Changes Impacting Medicare Reimbursements

From time to time, Congress has revised the Medicare statute and the formulas it establishes for the CLFS. The payment amounts under the Medicare fee schedules are important because they not only will determine our reimbursement under Medicare, but those payment amounts are also often used as a basis for payment amounts set by other governmental and private third-party payers. For example, state Medicaid programs are prohibited from paying more than the Medicare fee schedule limit for clinical laboratory services furnished to Medicaid recipients.

The Protecting Access to Medicare Act of 2014 ("PAMA"), enacted April 1, 2014 overhauls the CLFS payment methodology and imposes a market-based reimbursement system. PAMA provides that, in general payment for clinical diagnostic laboratory tests ("CLDTs") will be equal to the weighted median of private payer rates for the test, based on data reported by certain laboratories during a specified collection period. PAMA requires a similar rate adjustment and reporting requirement for advanced diagnostic laboratory tests ("ADLTs"). ADLTs are CDLTs furnished by a single laboratory, not sold for use by other entities, and meeting at least one of the following criteria:

- Analysis of multiple biomarkers of DNA, RNA or proteins combined with a unique algorithm to yield a single patient-specific result;

- Cleared or approved by the FDA; or

- Meets other similar criteria established by the Secretary of Health and Human Services.

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The tests we will offer will most likely be classified as CDLTs. We will however pursue ADLT status.

On June 23, 2016, the CLFS final rule entitled "Medicare Program: Medicare Clinical Diagnostic Laboratory Test Payment System" ("Final Rule") set out the details of the payment policy mandated by PAMA and set an effective date of January 1, 2018 for the shift in payment rates. PAMA and the Final Rule will significantly impact the way that laboratory tests are reimbursed by Medicare. CMS estimates that the Final Rule will result in a reduction of approximately $390 million, or 5.6%, in Medicare spending on clinical laboratory tests in federal fiscal year 2018 and nearly $4 billion over the course of 10 years

Beginning January 1, 2017 Medicare payment for any ADLT will be based on the list price or charge. After the test is commercially available for three quarters, the laboratory will be required to report payment and volume information and this data will be used to set payment for the test for the following year.

- If data shows that the list price was greater than 130% of the payment using established methodology, generally a weighted median, CMS will recoup the difference from the laboratory through a payment claw back.

- Payment will be updated annually based on the weighted median of commercial payer reimbursement.

Congress has proposed on several occasions to impose a 20% coinsurance charge on patients for CDLTs reimbursed under CLFS, which would require us to bill patients for these amounts. Because of the relatively low reimbursement for many CDLTs, in the event that Congress were to ever enact such legislation, the cost of billing and collecting for these services would often exceed the amount actually received from the patient and effectively increase our costs of billing and collecting.

Some Medicare claims may be subject to policies issued by the Medicare Administrative Contractor ("MAC") for California. CMS relies on a network of MACs to process Medicare claims, and MACs serve as the primary operational contact between the Medicare Fee-For-Service program and approximately 1.5 million health care providers enrolled in the program. The predecessor to the current California MAC, acting on behalf of many MACs, issued a Local Coverage Determination that affects coverage, coding and billing of many molecular diagnostic tests. Under this Local Coverage Determination, the MAC took the position that it would not cover any molecular diagnostic test unless the test is expressly included in a National Coverage Determination issued by CMS, or a Local Coverage Determination, or coverage article issued by the MAC. Denial of coverage for our diagnostic tests by the current California MAC, Noridian Healthcare Solutions, or reimbursement at inadequate levels, would have a material adverse impact on our business and on market acceptance of our planned diagnostic tests.

Private and Governmental Third Party Payers

Where there is a private or governmental third-party payer coverage policy in place, we will bill the payer and the patient in accordance with the established policy. Where there is no coverage policy in place, we will pursue reimbursement on a case-by-case basis. Our efforts in obtaining reimbursement based on individual claims, including pursuing appeals or reconsiderations of claims denials, could take a substantial amount of time, and bills may not be paid for many months, if at all. Furthermore, if a third-party payer denies coverage after final appeal, payment may not be received at all.

Reimbursement rates paid by private third-party payers can vary based on whether the provider is considered to be an "in-network" provider, a participating provider, a covered provider, an "out-of-network" provider or a non-participating provider. These definitions can vary among payers. An in-network provider usually has a contract with the payor or benefits provider. This contract governs, among other things, service-level agreements and reimbursement rates. In certain instances an insurance company may negotiate an in-network rate for our testing. An in-network provider may have rates that are lower per test than those that are out-of-network, and that rate can vary widely. Rates vary based on

the payer, the testing type and often the specifics of the patient's insurance plan. If a laboratory agrees to contract as an in-network provider, it generally expects to receive quicker payment and access to additional covered patients. However, it is likely that we will initially be considered an "out-of-network" or non-participating provider by payers who cover the vast majority of lives until we can negotiate contracts with these payers.

We cannot predict whether, or under what circumstances, payers will reimburse for all components of our tests. Full or partial denial of coverage by payers, or reimbursement at inadequate levels, would have a material adverse impact on our business and on market acceptance of our tests.

Direct Billing Laws and Other State Law Restrictions on Billing for Laboratory Services

Laws and regulations in certain states prohibit laboratories from billing physicians or other purchasers for testing that they order. Some states may allow laboratories to bill physicians directly but may prohibit the physician and, in some cases, other purchasers from charging more than the purchase price for the services, or may allow only for the recovery of acquisition costs, or may require disclosure of certain information on the invoice. In some cases, and if not prohibited by law or regulation, we may bill physicians, hospitals and other laboratories directly for the services that they order. An increase in the number of states that impose similar restrictions could adversely affect us by encouraging physicians to perform laboratory services in-house or by causing physicians to refer services to other laboratories that are not subject to the same restrictions.

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Government Regulation

Clinical Laboratory Improvement Amendments of 1988 and State Regulation

As a provider of laboratory testing on human specimens for the purpose of disease diagnosis, prevention, or treatment, we will be required to hold certain federal, state, and local licenses, certifications and permits to conduct our business. In 1988, Congress enacted CLIA, which established quality standards for all laboratories providing testing to ensure the accuracy, reliability and timeliness of patient test results regardless of where the test was performed. Our laboratory will obtain a CLIA certificate of accreditation. We also will be required to meet certain laboratory licensing and other requirements under state laws. Our laboratory will hold the required licenses from the applicable state agencies in the states in which we operate or from which we receive blood or urine samples for testing.

Under CLIA, a laboratory is defined as any facility that performs laboratory testing on specimens derived from humans for the purpose of providing information for the diagnosis, prevention or treatment of disease, or the impairment of, or assessment of health of human beings. CLIA requires that we hold a certificate applicable to the complexity of the categories of testing we perform and that we comply with certain standards. CLIA further regulates virtually all clinical laboratories by requiring that they comply with various operational, personnel, facilities administration, quality and proficiency testing requirements intended to ensure that their clinical laboratory testing services are accurate, reliable and timely. CLIA certification is also a prerequisite to be eligible to be reimbursed for services provided to state and federal health care program beneficiaries. CLIA is user-fee funded. Therefore, all costs of administering the program must be covered by the regulated facilities, including certification and survey costs.

Under CLIA, laboratory licensing requires a site inspection, review of standard operating procedures and verification that diagnostic results can be reproduced reliably across a number of different conditions. Before submitting for a license, extensive clinical testing, which is typically done in two phases, must be undertaken at a hospital or medical center to demonstrate optimal use, safety, and efficacy of the test in diagnosing a specific condition. Each clinical study is conducted under the auspices of an institutional review board that will consider, among other things, ethical factors, the safety of human subjects, and the possible liability of the institution.

Clinical studies are generally conducted in two phases. The first phase is Analytical Validation, which is done in the research laboratory and involves the replication of consistent results for the same sample across a spectrum of different conditions. Once the Analytical Validation is completed, the assay moves into Clinical Validation. In Clinical Validation, tests are run to confirm that consistent results for the same sample can be obtained in the actual laboratory that will conduct the commercial tests.

We will be subject to regular surveys and inspections to assess compliance with program standards. Laboratories performing high complexity testing are required to meet more stringent requirements than laboratories performing less complex tests.

CLIA and FDA Regulation of Diagnostic Tests

Our diagnostic tests will likely be classified as LDTs and consequently be governed under the CLIA regulations, as administered by CMS, as well as by applicable state laws. Historically, the FDA has exercised enforcement restraint with respect to most LDTs and has not required laboratories that offer LDTs to comply with FDA requirements for medical devices, such as registration, device listing, quality systems regulations, premarket clearance or premarket approval, and post-market controls. In recent years, however, the FDA has stated it intends to end its policy of enforcement restraint and begin regulating certain LDTs as medical devices. On October 3, 2014, the FDA issued two draft guidance documents, entitled “Framework for Regulatory Oversight of Laboratory Developed Tests (LDTs)” and “FDA Notification and Medical Device Reporting for Laboratory Developed Tests (LDTs)”, respectively, that set forth a proposed risk-based regulatory framework that would apply varying levels of FDA oversight to LDTs.

On January 13, 2017, the FDA issued a Discussion Paper on LDTs (“Discussion Paper”), which follows the FDAs late 2016 announcement that contrary to its earlier reports, it would not issue a final guidance on its proposed oversight of LDTs and allow for further public discussion on appropriate oversight. As it did in its 2014 guidance documents, the FDA continues to advocate a risk based approach to LDT oversight and proposes focusing on new and significantly modified high and moderate risk LDTs; however, new and significantly modified LDTs in certain categories would not be expected to comply with premarket review, quality systems, and registration and listing requirements unless necessary to protect public health. These exempt categories include low risk LDTs, LDTs for rare diseases, traditional LDTs, LDTs intended solely for public health surveillance, certain LDTs used in CLIA certified labs, and LDTs intended solely for forensic use. Based on the FDA’s guidance in the Discussion Paper, our products will likely not require FDA filing before launch. With respect to the postmarket surveillance of LDTs, the FDA’s Discussion Paper recommends that laboratories initially report serious adverse events for all tests except the exempted categories if tests, which include LDTs intended for public health surveillance, some stem cell/tissue/organ transplantation LDTs, and LDTs intended solely for forensic use. The Discussion Paper notes that while the report neither represents the formal position of the FDA and nor is it a final version of the LDT guidance documents published in 2014, it is hoped that its publication will continue to advance further public disclosure.

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Based on guidance set forth in the Discussion Paper, FDA premarket review of new and significantly modified LDTs could be phased-in over four years, however, to date no firm time commitments have been set. Nonetheless, the FDA may decide to regulate certain LDTs on a case-by-case basis at any time.

Failure to comply with applicable FDA regulatory requirements may trigger a range of enforcement actions by the FDA, including warning letters, civil monetary penalties, injunctions, criminal prosecution, recall or seizure, operating restrictions, partial suspension or total shutdown of operations, and denial of or challenges to applications for clearance or approval, as well as significant adverse publicity. We cannot predict the ultimate form or impact of any such FDA guidance and the potential effect on our diagnostic test services.

We cannot provide any assurance that FDA regulation, including premarket review, will not be required in the future for our diagnostic tests, whether through additional guidance or regulations issued by the FDA, new enforcement policies adopted by the FDA or new legislation enacted by Congress. It is possible that proposed legislation discussed above or other new legislation could be enacted into law, or new regulations or guidance could be issued by the FDA. Such new legislation may result in new or increased regulatory requirements for us to continue to offer our diagnostic tests or to develop and introduce new tests or services.

If premarket review, including approval, is required, our business could be negatively affected until such review is completed and clearance to market or approval is obtained. If we are selling any of our diagnostic tests when new FDA approval requirements are implemented, we may be required to suspend sales until we obtain premarket clearance or approval. If our diagnostic tests are allowed to remain on the market but there is uncertainty about the legal status of those tests, if we are required by the FDA to label them investigational, or if labeling claims the FDA allows us to make are limited, order levels for the use of our tests may decline and reimbursement may be adversely affected.

FDA regulations could also require, among other things, additional clinical studies and submission of a premarket notification or filing a Premarket Approval ("PMA") application with the FDA. For example, LDTs with the same intended use as a cleared or approved companion diagnostic are defined in FDA’s draft guidance as “high-risk LDTs (Class III medical devices)” for which premarket review would be required. This may include the use of our LDTs for screening patients for cancer. See the discussion of FDA regulation of medical devices below under In Vitro Diagnostics. If premarket review is required by the FDA, there can be no assurance that our diagnostic tests will be cleared or approved on a timely basis, if at all, nor can there any be assurance that labeling claims allowed by the FDA will be consistent with our intended claims or will be adequate to support continued adoption of and reimbursement for our tests. Compliance with FDA regulations would increase the cost of conducting our business, and subject us to heightened requirements of the FDA and penalties for failure to comply with these requirements. We may also decide voluntarily to pursue FDA premarket review of our diagnostic tests if we determine that doing so would be appropriate.

California State Laboratory Licensing

In addition to federal certification requirements of laboratories under CLIA, licensure will be required and maintained under California law for the San Francisco Bay Area based laboratory that we plan to establish. Such laws include standards for the day-to-day operation of a clinical reference laboratory, including the training and skills required of personnel and quality control. In addition, California laws mandate proficiency testing, which involves testing of specimens that have been specifically prepared for the laboratory.

We will not be permitted to perform diagnostic tests at our California CLIA laboratory until it is certified by the state, and if after certification our laboratory falls out of compliance with California standards, the California Department of Health Services (“DHS”) may suspend, restrict or revoke our license to operate our laboratory, assess substantial civil money penalties, or impose specific corrective action plans. Any such actions could materially affect our business.

Other States' Laboratory Licensing

Some states require licensure of out-of-state laboratories that accept specimens from those states. Our laboratories will need to pass various state inspections in order to get licensed to provide LDTs in each of state that requires licensure. In addition to the inspection requirements of the other states, Pennsylvania, Florida and Maryland have laws that require a certificate of compliance, and New York has its own special inspection requirements that must be met, in order to market our diagnostics in those states or to perform diagnostic tests on specimens received from patients residing in those states.

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In Vitro Diagnostics

In the future, we may elect to develop IVDs, which are regulated by the FDA as medical devices. Medical devices marketed in the United States are subject to the regulatory controls under CLIA, the Federal Food, Drug, and Cosmetic Act, and regulations adopted by the FDA. Some requirements, known as premarket requirements, apply to medical devices before they are marketed, and other requirements, known as post-market requirements, apply to medical devices after they are marketed.

The particular premarket requirements that must be met to market a medical device in the United States will depend on the classification of the device under FDA regulations. Medical devices are categorized into one of three classes, based on the degree of risk they present. Devices that pose the lowest risk are designated as Class I devices; devices that pose moderate risk are designated as Class II devices and are subject to general controls and special controls; and the devices that pose the highest risk are designated as Class III devices and are subject to general controls and premarket approval.

A premarket submission to the FDA will be required for some Class I devices, most Class II devices; and all Class III devices. Most Class I and some Class II devices are exempt from premarket submission requirements. Some Class I and most Class II devices may only be marketed after a 510(k) premarket notification, while a more extensive PMA is required to market Class III devices.

Until all regulatory requirements are phased in, our initial confirmatory diagnostics will not require FDA filing before launch. Since the tests are being developed as LDTs, the regulatory pathway that we will be following is the CLIA certification and inspection pathway.

If we elect to develop IVDs, our future screenings diagnostics may require a 510(k) submission or a PMA. In a 510(k) submission, the device sponsor must demonstrate that the new device is “substantially equivalent” to a predicate device in terms of intended use, technological characteristics, and performance testing. A 510(k) requires demonstration of substantial equivalence to another device that is legally marketed in the United States. Substantial equivalence means that the new device is at least as safe and effective as the predicate. A device is substantially equivalent if, in comparison to a predicate it (a) has the same intended use as the predicate and has the same technological characteristics as the predicate; or (b) has the same intended use as the predicate, has different technological characteristics, and the information submitted to FDA does not raise new questions of safety and effectiveness, and is demonstrated to be at least as safe and effective as the legally marketed predicate device.

A claim of substantial equivalence does not mean the new and predicate devices must be identical. Substantial equivalence is established with respect to intended use, design, energy used or delivered, materials, chemical composition, manufacturing process, performance, safety, effectiveness, labeling, biocompatibility, standards, and other characteristics. A device may not be marketed in the United States until the submitter receives a letter declaring the device substantially equivalent. If the FDA determines that a device is not substantially equivalent, the applicant may resubmit another 510(k) with new data, or request a Class I or II designation through the FDA’s de novo process that allows a new device without a valid predicate to be classified into Class I or II if it meets certain criteria, or file a reclassification petition, or submit a PMA.

A new 510(k) submission is required for changes or modifications to an existing approved device, where the modifications could significantly affect the safety or effectiveness of the device or the device is to be marketed for a new or different indication for use.

A PMA for Class III devices is the most stringent type of premarket submission. Before the FDA approves a PMA, the sponsor must provide valid scientific evidence demonstrating reasonable assurance of safety and effectiveness for the device’s intended use.

Submission of an application is no guarantee that the CMS or FDA will find it complete and accept it for filing. If an application is accepted for filing or licensing, following the CMS or FDA's review, the CMS or FDA may grant marketing approval, request additional information or deny the application if it determines that the application does not provide an adequate basis for approval.

Health Insurance Portability and Accountability Act

Under the Health Insurance Portability and Accountability Act ("HIPAA"), the Department of Health and Human Services ("HHS") has issued regulations to protect the privacy and security of protected health information used or disclosed by health care providers, such as us. HIPAA also regulates standardization of data content, codes and formats used in health care transactions and standardization of identifiers for health plans and providers. Penalties for violations of HIPAA regulations include civil and criminal penalties.

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CMS and the Office of Civil Rights issued a final rule in February 2014 to amend both the HIPAA and CLIA regulations. The final rule amended the HIPAA privacy rule to remove the CLIA laboratory exceptions, and as a result, HIPAA-covered laboratories are now required to provide individuals, upon request, with access to their completed test reports. Under the 2014 rule, CLIA laboratories and CLIA-exempt laboratories may provide copies of a patient's completed test reports that, using the laboratory's authentication process, can be identified as belonging to that patient. These changes to the CLIA regulations and the HIPAA Privacy Rule provide individuals with a greater ability to access their health information, empowering them to take a more active role in managing their health and health care. CLIA laboratories must create and maintain policies, procedures, and other documentation necessary to inform patients of the right to access laboratory test reports and how to exercise that right.

New laws governing privacy may also be adopted in the future. We will take steps to comply with all current health information privacy requirements of which we are aware and with which we must comply. However, we can provide no assurance that we will remain in compliance with diverse privacy requirements in all of the jurisdictions in which we do business. The current requirements may periodically change and could have an effect on our business operations if compliance becomes substantially more costly than under current requirements. Failure to comply with privacy requirements could result in civil or criminal penalties, which could have a materially adverse effect on our business.

Physician Referral Prohibitions

Under a federal law directed at "self-referral," commonly known as the Stark Law, there are prohibitions, with certain exceptions, on Medicare and Medicaid payments for laboratory tests referred by physicians who personally, or through a family member, have a "financial relationship"—including an investment or ownership interest or a compensation arrangement—with the clinical laboratory performing the tests. Several Stark Law exceptions are relevant to arrangements involving clinical laboratories, including: (1) fair market value compensation for the provision of items or services; (2) payments by physicians to a laboratory for clinical laboratory services; (3) certain space and equipment rental arrangements that satisfy certain requirements, and (4) personal services arrangements that satisfy certain requirements. The laboratory cannot submit claims to the Medicare Part B program for services furnished in violation of the Stark Law, and Medicaid reimbursements may be at risk as well. Penalties for violating the Stark Law include the return of funds received for all prohibited referrals, fines, civil monetary penalties and possible exclusion from the federal health care programs. Many states have comparable laws that are not limited to Medicare and Medicaid referrals.

Corporate Practice of Medicine

A number of states, including California, do not allow business corporations to employ physicians to provide professional services. This prohibition against the "corporate practice of medicine" is aimed at preventing corporations such as us from exercising control over the medical judgments or decisions of physicians. The state licensure statutes and regulations and agency and court decisions that enumerate the specific corporate practice rules vary considerably from state to state and are enforced by both the courts and regulatory authorities, each with broad discretion. If regulatory authorities or other parties in any jurisdiction successfully assert that we are engaged in the unauthorized corporate practice of medicine, we could be required to restructure our contractual and other arrangements. In addition, violation of these laws may result in sanctions imposed against us and/or the professional through licensure proceedings, and we could be subject to civil and criminal penalties that could result in exclusion from state and federal health care programs.

Federal and State Fraud and Abuse Laws

A variety of federal and state laws prohibit fraud and abuse. These laws are interpreted broadly and enforced aggressively by various state and federal agencies, including CMS, the Department of Justice, the Office of Inspector

General for HHS, and various state agencies. In addition, the Medicare and Medicaid programs increasingly use a variety of contractors to review claims data and to identify improper payments as well as fraud and abuse. These contractors include Recovery Audit Contractors, Medicaid Integrity Contractors and Zone Program Integrity Contractors. In addition, CMS conducts Comprehensive Error Rate Testing audits, the purpose of which is to detect improper Medicare payments. Any overpayments identified must be repaid unless a favorable decision is obtained on appeal. In some cases, these overpayments can be used as the basis for an extrapolation, by which the error rate is applied to a larger universe of claims, and which can result in even higher repayments.