

SIGNAL GENETICS, INC.
Form 10-K
March 21, 2016

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, D.C. 20549

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 2015

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: 001-36483

SIGNAL GENETICS, INC.

(Exact name of registrant as specified in its charter)

Delaware 47-1187261
(State or other jurisdiction of (I.R.S. Employer
incorporation or organization) Identification Number)

5740 Fleet Street, Carlsbad, California 92008
(Address of principal executive offices) (Zip Code)

Registrant's telephone number, including area code: (760) 537-4100

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

<u>Title of each class</u>	<u>Name of each exchange on which registered</u>
Common Stock, \$0.01 par value	The NASDAQ Capital Market

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

The aggregate market value of the voting stock held by non-affiliates of the registrant, based upon the closing sale price of the Common Stock on June 30, 2015 as reported on The NASDAQ Capital Market, was \$11.6 million. Shares of Common Stock held by each executive officer and director and by each person who owns 10% or more of the outstanding Common Stock have been excluded in that such persons may be deemed to be affiliates. This determination of affiliate status is not necessarily a conclusive determination for other purposes.

As of March 15, 2016, there were 10,709,080 shares of the registrant's Common Stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

None.

SIGNAL GENETICS, INC.

INDEX

	Page No.
PART I	
<u>ITEM 1. BUSINESS</u>	<u>1</u>
<u>ITEM 1A. RISK FACTORS</u>	<u>14</u>
<u>ITEM 1B. UNRESOLVED STAFF COMMENTS</u>	<u>38</u>
<u>ITEM 2. PROPERTIES</u>	<u>38</u>
<u>ITEM 3. LEGAL PROCEEDINGS</u>	<u>38</u>
<u>ITEM 4. MINE SAFETY DISCLOSURES</u>	<u>38</u>
PART II	
<u>ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES</u>	<u>39</u>
<u>ITEM 6. SELECTED FINANCIAL DATA</u>	<u>40</u>
<u>ITEM 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS</u>	<u>41</u>
<u>ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK</u>	<u>48</u>
<u>ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA</u>	<u>48</u>
<u>ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE</u>	<u>48</u>
<u>ITEM 9A. CONTROLS AND PROCEDURES</u>	<u>49</u>
<u>ITEM 9B. OTHER INFORMATION</u>	<u>49</u>
PART III	
<u>ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE</u>	<u>50</u>
<u>ITEM 11. EXECUTIVE COMPENSATION</u>	<u>55</u>
<u>ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS</u>	<u>63</u>

<u>ITEM 13.</u>	<u>CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS AND DIRECTOR INDEPENDENCE</u>	<u>64</u>
<u>ITEM 14.</u>	<u>PRINCIPAL ACCOUNTING FEES AND SERVICES</u>	<u>65</u>
PART IV		
<u>ITEM 15.</u>	<u>EXHIBITS AND FINANCIAL STATEMENT SCHEDULES</u>	<u>66</u>
	<u>SIGNATURES</u>	<u>69</u>

FORWARD-LOOKING STATEMENTS

All statements included in this Annual Report on Form 10-K (this “Annual Report”) that are not historical are forward-looking statements within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended (the “Exchange Act”). These forward-looking statements can generally be identified as such because the context of the statement will include words such as “may,” “will,” “intend,” “plans,” “believes,” “anticipates,” “expects,” “estimates,” “predicts,” “potential,” “continue,” “opportunity,” “goals,” or “should,” the negative of these words or words of similar import. Similarly, statements that describe our future plans, strategies, intentions, expectations, objectives, goals, or prospects are also forward-looking statements. These forward-looking statements are or will be, as applicable, based largely on our expectations and projections about future events and future trends affecting our business, and so are or will be, as applicable, subject to risks and uncertainties including but not limited to the risk factors discussed in this report, that could cause actual results to differ materially from those anticipated in the forward-looking statements. We caution investors that there can be no assurance that actual results or business conditions will not differ materially from those projected or suggested in such forward-looking statements. The forward-looking statements included in this Annual Report speak only as of the date of this Annual Report. Our views and the events, conditions and circumstances on which these future forward-looking statements are based, may change. We do not assume any obligation to update or revise any forward-looking statements, whether as a result of new information, future events or developments, or otherwise, except as may be required by the securities laws, and we caution you not to rely on them unduly. All forward-looking statements are qualified in their entirety by this cautionary statement.

PART I

Item 1. Business

We were founded in New York as a Delaware limited liability company in January 2010 under the name Myeloma Health LLC. Signal Genetics LLC was formed as a Delaware limited liability company in December 2010. Effective January 1, 2011, substantially all of the member interests in Myeloma Health LLC were exchanged for member interests in Signal Genetics LLC and Myeloma Health LLC became a subsidiary of the Company. Immediately prior to the pricing of our initial public offering, on June 17, 2014, Signal Genetics LLC converted from a Delaware limited liability company to a Delaware corporation (the “Corporate Conversion”). In connection with the Corporate Conversion, each unit of Signal Genetics LLC was converted into a share of common stock of Signal Genetics, Inc., the members of Signal Genetics LLC became stockholders of Signal Genetics, Inc. and Signal Genetics, Inc. succeeded to the business of Signal Genetics LLC and its consolidated subsidiaries. As used in this report, the words “we,” “us,” “our,” the “Company,” and “Signal Genetics” refer to Signal Genetics, Inc. and its wholly-owned subsidiaries.

Overview

We are a commercial stage, molecular genetic diagnostic company focused on providing innovative diagnostic services that help physicians make better-informed decisions concerning the care of their patients suffering from cancer. Our mission is to develop, validate and deliver innovative diagnostic services that enable better patient-care

decisions. The patient-care decisions we impact include the field of personalized medicine, wherein diagnostic tests guide treatment decisions with genetically-targeted therapies as well as traditional chemotherapy regimens. We hold an exclusive license in our licensed field to the intellectual property stemming from the renowned research on multiple myeloma (“MM”), performed at the University of Arkansas for Medical Sciences (“UAMS”).

MM is a hematologic, or blood, cancer that develops in the bone marrow and specifically affects the plasma cells of the bone marrow. Normal plasma cells produce immunoglobulins, otherwise known as antibodies, which help the body fight infection and disease. In MM, the normal plasma cells become malignant and inhibit the production of normal blood cells and antibodies, including red blood cells, white blood cells and blood platelets, and crowd the bone marrow with malignant plasma cells, which produce an abnormal antibody called a monoclonal protein (“M protein”). The hallmark characteristic of MM is a high level of M protein in the blood. MM can also cause soft spots in the bone known as osteolytic lesions. MM is the second most common blood cancer after non-Hodgkin’s lymphoma (“NHL”) and represents approximately 15% of all hematological malignancies. According to the American Cancer Society and the National Cancer Institute, approximately 26,850 new cases of MM were expected to be diagnosed in the United States in 2015 and approximately 11,240 deaths from MM were expected to occur in the United States in 2015. More Americans were expected to die from MM in 2015 than from any other blood cancer. Although a relatively rare disease, MM is responsible for 2% of all cancer deaths in the United States each year and will kill more Americans than melanoma, the deadliest form of skin cancer. There are an estimated 89,658 people currently living with MM in the United States. The five-year survival rate for people with MM is about 47%. The American Cancer Society estimates that the lifetime risk in the United States of getting MM is 1 in 143.

To date, there are no known causes of MM. The most significant risk factor for developing MM is age. According to Nature: International Weekly Journal of Science's supplement on MM published on December 15, 2011 in volume 480, page S-33 through S-80, or Nature's MM supplement, 96% of MM cases are diagnosed in people older than 45 years of age, and more than 63% are diagnosed in people older than 65 years of age. There are usually no early stage symptoms of MM and a suspicion of a MM diagnosis is often made incidentally through routine blood tests which reveal low numbers of red blood cells and high levels of protein. Once diagnosed, MM is classified into one of three categories in a process known as staging. Staging is the process of determining how widespread or advanced the cancer is. Under the International Staging System ("ISS"), MM is classified into three stages based upon the presence of serum beta-2 microglobulin and serum albumin, which are blood proteins that are measured through a blood test. Staging is the key factor in a physician's choice of treatment for a patient and that patient's outlook or prognosis, often framed as progression free survival ("PFS") or overall survival ("OS"). Prognosis is typically based on the existence of different signs, symptoms and circumstances. Certain laboratory and clinical findings, or prognostic indicators, provide important information for MM, including when treatment should begin and what treatments to use, based upon a patient's individual prognosis and risk for relapse. However, the experts caring for MM patients have been burdened by a staging system that predates and thus fails to capture the rich body of new genomic information that has been shown to assist in the staging process. Similar genetic information has proven transformational in a number of solid tumor types, including breast, colon and lung cancer. In each case, specific genetic determinants enable doctors to identify patients who are likely to respond to genetically targeted therapies, resulting in better outcomes for these patients, including a higher rate of survival. According to the National Cancer Institute, these benefits have not yet been recognized in MM treatment. The traditional approach in MM treatment which utilizes cytogenetic techniques, such as karyotyping and fluorescent in-situ hybridization ("FISH"), for staging may not accurately stage MM patients or accurately assess the risk of relapse. Perhaps the greatest shortcoming of the current staging system for MM is its inability to classify MM patients into high and low risk prognosis groups. A tool that can further define risk-stratification by classifying MM patients in this manner would better inform physicians when to treat and what drugs to treat patients with, potentially improving health outcomes in MM patients. We believe a more comprehensive, systematic approach utilizing current genetic technologies is necessary to meet this unmet medical need.

Our flagship diagnostic service is the Myeloma Prognostic Risk Signature, or MyPRS[®] test. The MyPRS[®] test is a microarray-based gene expression profile ("GEP"), assay that measures the expression level of specific genes and groups of genes that are designed to predict an individual's long-term clinical outcome/prognosis, giving a basis for personalized treatment options and helping physicians classify MM patients into either high or low risk groups. The MyPRS[®] test provides a whole-genomic expression profile of a patient's MM. The GEP is a genetic fingerprint of a cancer, with each cancer being unique, just as each fingerprint is unique. Many recent studies show that the GEP of cancerous tumors makes personalized treatment possible, and our MyPRS[®] test is the first genetic test to be developed specifically for MM according to the 2007 John Shaughnessy paper in the journal Blood (A validated gene expression model of high-risk multiple myeloma is defined by deregulated expression of genes mapping to chromosome 1. Mar 15;109(6):2276-84. Epub 2006 Nov 14). MyPRS[®] is designed to be used at the time of initial MM diagnosis and also when the patient has experienced a relapse as an aid to physicians in selecting the optimal treatment regimen for each patient's unique condition. Specifically, the test helps allow:

- risk stratification to help distinguish patients with indolent MM that may not need treatment from those patients with aggressive MM that requires more aggressive treatment; and
- identification of important genomic alterations that allow for MM sub-classification that may affect the therapy selection, and potentially enable a personalized medicine approach.

Our Services

We offer our MyPRS[®] test in our approximately 2,800 square foot state-of-the-art laboratory located in Little Rock, Arkansas, which is certified under the Clinical Laboratory Improvement Amendments of 1988 (“CLIA”) and accredited by the College of American Pathologists (“CAP”), to perform high complexity testing. We are licensed to sell our test in all 50 states. We are dedicated to making our extensively validated diagnostic services available to all patients who need them.

In addition, we are exploring, and peer-review studies are being conducted on, the use of our MyPRS[®] test as an indicator of progression to MM in patients with either smoldering multiple myeloma (“SMM”), or monoclonal gammopathies of unknown significance (“MGUS”), the precursor conditions to MM. There is, however, currently no projected timeline for our use of MyPRS[®] in these patients. For a discussion of MyPRS[®] in these patients see “— Market Opportunities,” below.

Over the next 12 to 18 months, we intend to expand our test menu by adding tests that are used to help manage MM patients. There is a broad array of molecular and cytogenetic testing modalities that are utilized in the management of patients with MM, such as conventional cytogenetics, FISH, molecular tests, M protein serum test and flow cytometry (especially in the context of minimum residual disease testing for MM therapy response). During 2015, we launched both RNA sequencing and next generation DNA sequencing services for research use only to assist our research collaborators, including pharmaceutical companies, in further characterizing their MM patients enrolled in clinical trials.

Market Opportunities

Over the past several decades, improved awareness and diagnostic testing technologies have led to an increase in the early diagnosis of cancer. Although the goals of these efforts were to decrease cancer mortality, national data demonstrate significant increases in early-stage disease, without a proportional decline in later-stage disease. What has emerged amongst clinicians and researchers has been an appreciation of the complexity of cancer. Cancers are heterogeneous and do not follow a uniform course. In some cases, cancer can lead to severe disease and death, while in other cases it is indolent. Unfortunately, identifying those patients who will likely succumb to non-cancer related causes, or comorbidities, is difficult.

Before 1990, treatment of MM was limited to the use of melphalan (a chemotherapeutic agent) and prednisone (a steroid), which were of marginal effectiveness. In 1986, high dose dexamethasone (a corticosteroid), which is used to induce plasma cell lysis, was introduced and in the early 1990s, induction therapy with vincristine, doxorubicin (a chemotherapeutic agent) and dexamethasone, followed by stem cell transplant after high dose melphalan was introduced and resulted in longer term remissions but patients always relapsed. Then, in 1999, thalidomide was added to existing regimens for MM. The first clinicians to attempt the use of thalidomide in the treatment of MM were at the UAMS. The initial use of thalidomide ultimately led to the development of Revlimid®, Celgene's blockbuster drug that is now part of most front-line therapies for the treatment of MM. In 2006, Velcade® was approved and added to existing regimens. Thalomid®, Revlimid® and Velcade® are now considered cornerstones of therapy in addition to stem cell transplant after bone marrow ablation.

Although new treatments for patients with MM have become available over the last 10 years, we do not believe that these treatments have provided any significant benefits in overall survival — especially in the high risk patient population. In part, this is because MM is a disease with significant tumor heterogeneity at the genetic level. Specialists in MM have long recognized the need for diagnostic tests that accurately identify the mutations and overarching genotype of each patient to inform risk stratification, prognosis and choice of therapy. Because it is impossible to use classic staging modalities such as clinical factors and cell morphology (the microscopic review of tumor material by a pathologist) to classify MM, physicians use plasma cell labeling indices, chemical markers, imaging studies and genetic abnormalities at the chromosomal level (e.g., cytogenetics) to better predict prognosis. Unfortunately, these tests provide limited information as to a particular MM patient's prognosis and response to treatment. With the use of MyPRS® GEP, it has become possible to go beyond morphological and chromosomal level analysis and identify the individual MM genomic profile of each individual patient.

Like many forms of cancer, MM can present as asymptomatic, even in advanced stages. MM begins as the precursor condition, MGUS. It is estimated that more than 3% of the population of the United States 50 years of age or older have MGUS. Characterized by an excess of particular immunoglobulins or M proteins in the serum or urine with less than 10% plasma cells in the bone marrow, MGUS is not itself harmful to health. But every year, 1% of MGUS patients will progress to MM.

Aside from the precursor condition, MGUS, MM exists on a spectrum from asymptomatic or SMM to full-blown MM. Collectively, these precursor conditions, MGUS and SMM, are referred to as AMG. Preventative treatment of every AMG patient is not a viable option. As noted in The Disperenziari paper (Blood October 2013), along with the prohibitive expense, many doctors worry that they could do more harm than good if they treat otherwise healthy people, the vast majority of whom will never develop MM. A 1988 clinical study discussed in Nature's MM supplement, using the best treatments available at the time, concluded that treating patients even at the smoldering stage caused unnecessary side effects with no survival benefit.

The applicability of our test for use in predicting MM progression from AMG could create a substantial increase in the potential patient population eligible for MyPRS® testing and as such represents an important pillar of our growth strategy. We estimate the total potential MM testing market in the United States at approximately 40,000 patients per year, including newly diagnosed and relapsed patients. We believe we currently service just over 3% of this market.

We estimate that the addition of an AMG progression indication feature for the MyPRS[®] test could expand the MyPRS[®] addressable market in the United States to more than 140,000 patients per year. As a specialty focused diagnostic laboratory company, we hope for such opportunities to expand our service offerings for the benefit and convenience of physicians and patients.

Our Competitive Strengths

Differentiated value proposition of the MyPRS[®] test

We believe the MyPRS[®] test is one of the most extensively validated molecular prognostic assays on the market today. There are more than 30 peer-reviewed scientific publications that substantiate the clinical validity and utility of the MyPRS[®] test. MyPRS[®] is the only GEP-based prognostic assay commercially available in the United States which may be used to determine which patients have a high-risk form of MM.

Additionally, the MyPRS[®] test provides oncologists with the molecular subtype of each patient's particular form of MM. Molecular subtypes can be used to further stratify the level of risk severity of a patient's MM as well as assist the physician in choosing the most appropriate therapy while potentially avoiding therapies that may be less beneficial or harmful.

Furthermore, MyPRS[®] provides a virtual karyotype (a characterization of the chromosomal complement of an individual or a species, including number, form and size of the chromosomes), that can identify cytogenetic abnormalities in patients with MM. The accuracy of this method was validated against a range of conventional cytogenetic techniques and was shown to have a concordance of 89%. Certain cytogenetic abnormalities are commonly used, along with clinical and cell biology parameters in the traditional work up of MM patients for determining disease stage and to help guide therapy decisions for patients. The virtual karyotype algorithm in MyPRS[®] was designed to be an alternative to conventional methods that can be time consuming, expensive, subjective and can often fail to provide results due to the difficulties encountered when attempting to culture myeloma cells.

Pharmaceutical Services

There are currently over 300 new therapies in development for MM. Many of the pharmaceutical and large biotechnology companies have ongoing development programs for new compounds and combinations of existing drugs including Celgene, Takeda, Novartis, Karyopharm, Pharmacyclics, Janssen and Roche.

We believe that MyPRS[®] offers an attractive value proposition for companies developing therapies for MM by its ability to stratify high-risk patients likely refractory to current standard of care and to identify a patient's molecular subtype which assists physicians in determining the most appropriate therapy or class of drugs for each patient. In addition, we have analyzed over 20,000 patients with MyPRS[®] and have the gene expression data available to assist companies in identifying the appropriate patient population for new compounds and combination therapies.

We executed master service agreements with two leading pharmaceutical companies in 2015. Under these agreements, MyPRS[®] is being run across multiple clinical trials in connection with the development of novel treatments for patients with MM.

Relationship with University of Arkansas, leader in the study and treatment of MM

We are the exclusive licensee to the intellectual property developed at UAMS's Myeloma Institute ("MI"), in our licensed field. MI is one of the largest centers in the world dedicated solely to MM and related diseases as well as to prevention and management of treatment-related consequences, including myelodysplastic syndrome ("MDS") and acute myelogenous leukemia (AML). UAMS developed a novel "Total Therapy" approach, designed as a first line treatment for MM that includes a full array of treatment modalities. This approach is considered, by many in the oncology community, to have achieved positive results, particularly in patients diagnosed with low-risk MM who are treated at UAMS MI. A number of treatment improvements for MM patients were first discovered at MI. The physicians at MI routinely utilize our MyPRS[®] test to identify patients who may be eligible for the provision of "Total Therapy."

We are the exclusive provider of GEP-based testing to UAMS. UAMS has a thirty-year history of clinical and research knowledge and experience. UAMS has treated more than 10,000 patients since the program's inception in 1989. UAMS has amassed more than 10,000 gene array samples, many of which were used to discover and validate the MyPRS[®] test. More than 90% of patients who are treated at UAMS continue to be actively followed by UAMS over the course of their lifetime — many patients have been followed for more than 20 years.

Because of our exclusive relationship with UAMS, we are uniquely positioned to benefit from the breadth of clinical research and expertise developed at UAMS. We intend to continue to use this relationship to improve our MyPRS[®] test and develop additional indications for the MyPRS[®] test, as well as additional tests. Our relationship with UAMS also provides us with credibility within the oncology community beyond that related to the MyPRS[®] validation we have received in published articles, and we benefit from this association in our pursuit of additional collaborations with leading universities and research institutions.

Revenue sourced from or through UAMS accounted for 54% and 84% of our net revenue for the years ended December 31, 2015 and 2014, respectively. The decrease is due to the decrease in research funds available at UAMS for such programs. We expect continued declining revenue from the UAMS research programs.

Our substantial proprietary estate that protects our exclusive access to the MyPRS[®] test

We use our trademark of Signal Genetics, Inc.TM and our registered trademark MyPRS[®] in this Annual Report. This report may also refer to trade names and trademarks of other organizations.

We currently license, or own outright, 14 issued patents (12 issued U.S. patents, one issued European patent validated in 9 countries: Switzerland, Germany, Denmark, Spain, France, United Kingdom, Italy, Netherlands, and Sweden, and one issued Japanese patent with various expiration dates ranging from 2022 to 2030) and 11 pending patent applications, many of which protect and defend our exclusive ability to market the MyPRS[®] test as well as additional proprietary tests and treatments. We also have six registered U.S. trademarks to further differentiate our products and services in the marketplace.

There are two issued U.S. patents related to the MyPRS[®] test, which form the basis of our right to exclude others from practicing the MyPRS[®] test. The patents claim methods of gene expression-based classification for MM using RNA from plasma cells, methods of identifying groups of genes that can distinguish normal and MM plasma cells by isolating RNA from CD138 positive plasma cells and identifying differentially expressed genes, methods of diagnosing MM by examining mRNA levels or chromosomal translocations of particular genes from plasma cells, methods of determining the prognosis of a human multiple myeloma patient by measuring gene expression levels of multiple genes from plasma cells, and methods of determining the prognosis of a MM patient by determining the copy number of the CKS1B gene in plasma cells. CKS1B is one of the genes in the 70 gene signature.

In addition to the issued U.S. patents, we have one issued Japanese patent and several pending patent applications in the United States and abroad directed to other aspects of the MyPRS[®] test. For example, the Japanese patent provides methods for examining the susceptibility of a subject for transformation from a low-risk to a high-risk MM by measuring gene expression levels of multiple genes expressed from plasma cells isolated from the subject. A Canadian application and an issued European counterpart patent of one of the five issued U.S. patents (U.S. Patent No. 8,843,320) describe the full 70 gene signature used in the MyPRS[®] test. Another pending U.S. application provides methods of prognosing subjects with MGUS using the 70 gene signature. We expect that additional advances will come out of our ongoing work and form the basis of additional intellectual property to protect and refine the MyPRS[®] test, through new patent filings, trademarks, trade secrets, and copyrights.

Focus on the leading academic hospitals in the United States where a large portion of MM patients are treated

We currently focus our sales efforts exclusively on leading academic research hospitals and clinics throughout the United States. Given our limited selling and marketing capabilities, focusing our sales efforts on these academic research hospitals and clinics provides an efficient way to reach the largest segment of MM patients with our limited resources. Selling into academic research hospitals and clinics is a complex process that requires technical knowledge and the ability to engage in discourse to convince technical and administrative stakeholders to adopt new diagnostic tests or therapies. Our current commercial team is well versed in the science and technology behind our MyPRS[®] test. We will continue to grow our commercial organization with expertise necessary to interface successfully with these institutions.

The extensive scientific evidence that substantiates the MyPRS[®] test is a key enabler for our sales effort that affords us access to the thought leaders within these institutions. The relationships that we build with the thought leaders at leading academic hospitals is a direct result of the quality of our science and the quality of our services and helps to secure continued access to these accounts and the MM patients they treat. It also affords us the opportunity to expand our offerings as we add additional services to our test menu.

Early success in establishing positive reimbursement coverage for MyPRS[®]

We successfully obtained a positive Local Coverage Determination (“LCD”), for MyPRS[®] in March 2011 from the Arkansas Medicare Administrative Contractor (“MAC”), which at the time was Pinnacle Medical Services. The current MAC is Novitas Health Solutions. We have also received reimbursement approval from Blue Cross Blue Shield of Arkansas and we are an in-network provider to their patient population. We anticipate that our managed care team, which includes our recently added Chief Medical Officer, as of September 2015, and the continued development of our clinical validity and utility dossier, we will be able to achieve positive coverage determinations from a number of the major third-party payors in the United States. However, those efforts may take quite some time and may not be successful. In the meantime, we have executed agreements with eleven Preferred Provider Networks (“PPO Networks”) to facilitate our reimbursement from third-party payors.

Experienced oncology-centered laboratory

Our specimens are tested and interpreted by highly qualified oncology-focused laboratory professionals with more than 70 years of cumulative experience with gene expression-based diagnostic testing technology. Because our clinical staff is highly specialized in oncology, we believe we are better positioned to consult with our oncologist customers to help them derive maximum value from the diagnostic and prognostic data generated by our tests.

Our Growth Strategy

Our goal is to deliver innovative diagnostic services that enable physicians to make better-informed treatment decisions regarding the care of their cancer patients. We intend to do this by:

- Expanding the U.S. market penetration of our MyPRS[®] test by increasing the geographic coverage of our commercial organization,;
- Broadening the base of health care insurance companies that have approved reimbursements for MyPRS[®];
- Expanding the diagnostic indications for MyPRS[®] to include AMG, the precursor conditions to MM;
- Pursuing additional collaborations with pharmaceutical companies who focus on developing therapies to treat MM and its precursor disease;
- Expanding our information technology infrastructure to further improve our customer service experience;
- Continuing to leverage our relationship with UAMS via our exclusive license agreement;
- Expanding our test offering with the addition of other molecular tests useful to physicians who care for MM patients;
- Expanding and leveraging our capabilities into additional blood cancer indications;
- Pursuing additional collaborations, mergers and acquisitions, and in-licensing to expand our service offering; and
- Continuing to reduce the costs associated with the development, manufacture and interpretation of our proprietary genomic tests and services.

Competition

The primary competition for our MyPRS[®] test stems from the use of older diagnostic technologies to assess patient prognosis and to define high risk and low risk MM patients. These older technologies include various serum markers, karyotype analysis and FISH probes. Several independent groups have assessed the use of GEP versus various conventional methodologies and these studies have been published in peer-reviewed journals. For a select list of these publications, please visit our website at www.signalgenetics.com in the “Publications” section under the “Physician Resources” tab. It is our experience that whenever MyPRS[®] is compared to conventional techniques, the MyPRS[®] test shows superior ability to predict patient outcome. We believe that an active educational-based marketing campaign and additional sales personnel to deliver the message to potential new clients is needed to drive MyPRS[®] adoption by educating physicians as to the limitations of conventional testing modalities and the added benefits of MyPRS[®] testing. Additionally, there are a number of independent clinical studies that are underway that continue to compare our MyPRS[®] test to various conventional techniques, and we believe these new studies will also demonstrate the superiority of our MyPRS[®] test to predict patient prognosis. However, we cannot be sure that the data will support the superiority of MyPRS[®] and even if there is support, physicians may not adopt use of MyPRS[®] by incorporating it in to their molecular diagnostic work up of MM or AMG patients.

Another source of competition for our MyPRS[®] test stems from other scientific teams attempting to develop GEP signatures utilizing other genes or a subset of the genes utilized in the MyPRS[®] test. Two signatures of note include the French IFM-15 gene signature and the Netherlands EMC-92 gene signature which have been studied by independent groups and compared to the UAMS GEP test, MyPRS[®]. Based on previous head-to-head comparisons, we believe that the MyPRS[®] test is a superior predictor of patient outcome compared to any other published gene expression signature. However, there is no guarantee that in the future a GEP will not be commercially available that is superior to MyPRS[®]. If that happens, our commercialization efforts could be severely hampered.

We are not currently aware of any company attempting to bring GEP based tests into the U.S. market. Additionally, we believe our intellectual property portfolio will provide protection for our exclusive ability to market GEP tests for MM in the U.S. Our success to date in establishing reimbursement coverage for our MyPRS[®] test may provide an additional competitive barrier to any new U.S. market entrant attempting to use GEP to predict prognosis in MM patients. This is because we believe any such test would have to be supported by evidence showing clinical validity and clinical utility that is of the same strength as the evidence supporting MyPRS[®]. Lastly, we are not aware of any pending clinical research utilizing a GEP to predict conversion from AMG to MM other than the SWOG study that used the MyPRS[®] test. However, there may be other academic or industry based scientists who are developing new genetic expression based predictive assays or other novel technology based assays that will be superior to MyPRS[®] test in predicting risk in patients with MM and/or AMG.

We compete largely on the basis of the quality of our tests, the significant number of peer-reviewed scientific publications that support the clinical validity and utility of our MyPRS[®] test, our turnaround time, the convenience of ordering our tests and the innovation of our results delivery platform.

We provide services in a segment of the health care industry that is highly fragmented and extremely competitive. Any failure to respond to technological advances and emerging industry standards could impair our ability to attract and retain clients. This industry is characterized by rapid technological change. Our actual and potential competitors in the United States and abroad may include biotechnology, genomic and diagnostic companies such as Novartis, Cancer Genetics, Inc. and NeoGenomics, Inc., large clinical laboratories, universities and other research institutions. Many of our potential competitors have considerably greater financial, technical, marketing, research and other resources than we do, which may allow these competitors to discover important information and develop technology before we do. It is anticipated that competition will continue to increase due to such factors as the potential for commercial applications of biotechnology and the continued availability of investment capital and government funding for cancer-related research. Our competitors may succeed in developing diagnostic products that are superior to our tests and technologies, including our pipeline products. Also, our competitors may succeed in developing technologies, products or services that are more effective than those that will be developed by us or that would render our technology or product candidates less competitive or obsolete.

In addition, our goal is to develop diagnostic tests and other services that impact the treatment of MM and other cancers. If those treatments change, it is possible that the demand for our services and products could significantly decline or cease altogether. The development of new or superior competing technologies, products or services, or a change in the treatment of MM and other cancers, could affect our competitive position and harm our business. Moreover, these competitors may offer broader services and/or product lines and have greater name recognition than us and may offer discounts as a competitive tactic.

Additionally, competitors may succeed in developing products and/or services that are approved by the FDA and/or they may market technologies, products or services that are more effective or commercially attractive than our tests and services or that render our technologies and current or potential tests and other services obsolete. Competitors may also develop proprietary positions that may prevent us from commercializing, or continue to commercialize current and future product candidates.

We also face competition from companies such as Genoptix, Inc. (a Novartis AG company), Neogenomics, Inc., Cancer Genetics, Inc., Bio-Reference Laboratories (a division of OPKO Health, Inc.), Integrated Genetics (a LabCorp Specialty Testing Group) and Foundation Medicine, Inc., which offer products or services or have conducted research to develop genetic profiles, or genetic or protein biomarkers for various cancers. Additionally, projects related to cancer genomics have received increased government funding, both in the United States and internationally. As more information regarding cancer genomics becomes available to the public, we anticipate that more products aimed at predicting patient outcome as well as identifying targeted treatment options will be developed and that these products may compete with ours. In addition, competitors may develop their own versions of our tests in countries where we did not apply for patents or where our patents have not issued and compete with us in those countries, including promoting the use of their test(s) by physicians or patients in other countries.

Research and Development Program

Research and development is crucial to our ongoing growth as we seek to expand our series of diagnostic tests for use by physicians that treat MM and other cancer patients. Our research and development expenses were \$1.0 million and \$347,000 for the years ended December 31, 2015 and 2014, respectively, representing 39% and 8% of our net revenue for the years ended December 31, 2015 and 2014, respectively. Major components of our research and development expenses include supplies and reagents for our research activities, personnel costs, occupancy costs, equipment warranties and service, insurance, consulting, and clinical research sponsorship. We are also investing in clinical research studies to further validate the clinical utility of MyPRS[®] to predict the risk that a patient with AMG would progress to developing MM and to facilitate the development and clinical utility validation of additional genetic characterization of MM patients. We expect research and development expenses to increase as we work to develop additional diagnostic tests and services or add indications, including new testing modalities, and to study additional diagnostic and prognostic indicators for patients suffering from MM and its precursor conditions AMG, as well as other hematolymphomas. In the future, we expect research and development expenses to increase as we work to develop additional tests and services and add indications to our MyPRS[®] test. We cannot estimate the amounts we will need to invest in order to achieve the new indications or new services, nor do we know if we will be successful in these endeavors.

Governmental Regulation

Our business is subject to extensive laws and regulations, the most significant of which are summarized below.

Clinical Laboratory Improvement Amendments

We are subject to CLIA, which is administered by CMS, and extends federal oversight to virtually all clinical laboratories by requiring certification by the federal government or by a federally-approved accreditation agency.

Under CLIA, a laboratory is defined as any facility which 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. CLIA requires that we hold a certificate applicable to the type of work we perform and comply with certain standards. CLIA further regulates virtually all clinical laboratories by requiring compliance with various operational, personnel, facilities, administration, quality and proficiency requirements intended to ensure that their clinical laboratory testing services are accurate, reliable and timely. CLIA certification is a prerequisite to being eligible to bill for services provided to governmental payor 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.

CLIA has specific conditions for certification. CLIA is intended to ensure the quality and reliability of clinical laboratories, including the accuracy, reliability and timeliness of patient test results performed in clinical laboratories in the United States, by mandating specific standards in the areas of personnel qualification, administration participation in proficiency testing, patient test management, quality control, quality assurance and inspections. CLIA regulations contain guidelines for the qualification, responsibilities, training, working conditions and oversight of clinical laboratory employees. In addition, specific standards are imposed for each type of test that is performed in a laboratory. The categorization of commercially marketed in vitro diagnostic tests under CLIA is the responsibility of the FDA. The FDA will assign commercially marketed test systems into one of three CLIA regulatory categories based on their potential risk to public health. Tests will be designated as waived, of moderate complexity or of high complexity. CLIA and the regulations promulgated thereunder are enforced through quality inspections of test methods, equipment, instrumentation, materials and supplies on a periodic basis. The sanction for failure to comply with CLIA requirements may be suspension, revocation or limitation of a laboratory's CLIA certificate, which is necessary to conduct business, as well as significant fines and/or criminal penalties. If a laboratory is certified as "high complexity" under CLIA, the laboratory is permitted to obtain analyte specific reagents, or ASRs, which are commercially marketed products that function as the building blocks of in vitro diagnostic tests and in-house diagnostic tests known as "home brews." We received our CLIA certificate as a "high complexity" laboratory in 2011. Our current CLIA certificate renewal period began April 14, 2015 and will expire on April 13, 2017. Loss of our CLIA certification, change in CLIA or CLIA regulations or in the interpretation thereof, could have a material adverse effect on our business.

New York State Laboratory Licensing

New York state laws and regulations also establish standards for the day-to-day operations of clinical laboratories, including physical facility requirements and equipment and quality control. New York standards include proficiency testing requirements, even for a laboratory not located within the state. In addition, the New York Department of Health separately approves certain LDTs offered in New York State. In June 2014, following our initial public offering, we obtained the requisite approvals for our LDTs in New York. Such license expires in June 2016. We expect to renew the license before expiration.

Other States' Laboratory Testing

In addition to New York, certain other states, including California, Florida, Maryland, Pennsylvania, and Rhode Island require that we hold licenses to test specimens from patients residing in those states even though we are physically located in Arkansas. We have obtained licenses in these states and believe we are in material compliance with their applicable licensing laws, and will continue to pursue license renewals, as required.

From time to time, other states may require out of state laboratories to obtain licensure in order to accept specimens from such state. If we identify any other state with such requirements or if we are contacted by any other state advising us of such requirements, we intend to follow instructions from the state regulators as to how we should comply with such requirements.

Other Laboratory Regulations

Our clinical operations are also subject to regulation under state laws that may be more stringent than CLIA. State clinical laboratory laws generally require that laboratories and/or laboratory personnel meet certain qualifications. State clinical laboratory laws also generally require laboratories to specify certain quality controls and maintain certain records. For example, California requires that we maintain a state issued license and comply with California standards for our laboratory operations, including the standards for laboratory personnel and quality control. Additional states may require similar licenses in the future. Potential sanctions for violation of these state requirements include significant fines and the suspension or loss of various licenses, certificates and authorizations, which could adversely affect our business and results of operations. Finally, we may be subject to regulation in foreign jurisdictions, including in Europe and Asia, if we expand offering of our tests or distribution of our tests internationally.

HIPAA Compliance and Privacy Protection and the HITECH Act

HIPAA and its implementing regulations established comprehensive federal protection for the privacy and security of health information. The HIPAA standards apply to three types of organizations, or “Covered Entities”: health plans, health care clearing houses, and health care providers who conduct certain health care transactions electronically, or Standard Transactions. Covered Entities must have in place administrative, physical and technical safeguards to protect against the misuse of individually identifiable health information, or PHI. Additionally, some state laws impose privacy and security protections more stringent than HIPAA’s and some states impose privacy and security obligations specifically applicable to clinical laboratories. Additionally, many states have implemented data breach laws requiring additional security measures for certain types of PHI and also public notification of the theft, breach or other loss of personal information. There are also international privacy laws, such as the European Data Directive and various national laws implementing the Data Directive, that impose restrictions on the access, use, and disclosure of health information and other types of identifiable personal information. All of these laws may impact our business. We are a Covered Entity subject to the HIPAA regulations because our testing services are reimbursable by insurance payors and we conduct Standard Transactions. We have an active program designed to address HIPAA regulatory compliance. This program will likely require periodic updating to comply with amendments to HIPAA. Regardless of our own Covered Entity status, HIPAA presently applies to many of the facilities and physicians with whom we do business and controls the ways in which we may obtain tissue specimens and associated clinical information from those facilities and physicians. We believe we have taken the steps required for us to comply with applicable health information privacy and confidentiality statutes and regulations under both federal and applicable state jurisdictions. However, we may not be able to maintain compliance in all jurisdictions where we do business. Our failure to comply with these privacy laws or significant changes in the laws restricting our ability to obtain tissue specimens and associated patient information could significantly impact our business and our future business plans.

Additionally, the HITECH Act and the regulations promulgated thereunder by the HHS require HIPAA covered entities, including clinical laboratories, to provide notification to affected individuals and to the Secretary of HHS, following discovery of a breach of unsecured PHI. In some cases, the HITECH Act requires covered entities to provide notification to the media of breaches. In the case of a breach of unsecured PHI at or by a business associate of a covered entity, the HITECH Act requires the business associate to notify the covered entity of the breach. The HITECH Act requires the Secretary of HHS to post on the HHS website a list of covered entities that experience breaches of unsecured PHI involving more than 500 individuals. The HITECH Act made other changes relating to the HIPAA privacy and security rules, including, among others, establishing that, effective February 17, 2010, the HIPAA security and certain privacy regulations apply directly to business associates and, consequently, that a business associate’s violation of the HIPAA regulations may result in government enforcement action directly against the business associate or the covered entity with whom the business associate contracts depending upon the nature of that business relationship. We contract with business associates to provide certain services regulated by the HIPAA regulations and therefore must comply with the HIPAA regulations governing those business relationships.

In summary, we are required to comply with laws governing the transmission, security and privacy of health information that require significant compliance costs, and any failure to comply with these laws could result in material criminal and civil penalties.

Federal and State Physician Self-referral Prohibitions

We are subject to the Stark Law, and restrictions under California's Physician Ownership and Referral Act, or PORA. These restrictions prohibit us from billing a patient or any governmental or private payor for any test when the physician ordering the test, or any member of such physician's immediate family, has an investment interest in or compensation arrangement with us, unless the arrangement meets an exception to the prohibition.

Both the Stark Law and PORA contain an exception for referrals made by physicians who hold investment interests in a publicly traded company that has stockholders' equity exceeding \$75 million at the end of its most recent fiscal year or on average during the previous three fiscal years, and which satisfies certain other requirements. In addition, both the Stark Law and PORA contain an exception for compensation paid to a physician for personal services rendered by the physician. In the future we may develop compensation arrangements with other physicians for personal services. We will structure these arrangements with terms intended to comply with the requirements of the personal services exception to Stark Law and PORA and other applicable laws.

However, we cannot be certain that regulators would find these arrangements to be in compliance with Stark Law, PORA or similar state laws. If we are deemed out of compliance by the applicable regulators, we would be required to refund any payments we receive pursuant to a referral prohibited by these laws to the patient, the payor or the Medicare program, as applicable.

Penalties for a violation of the Stark Law include: refunds of amounts collected by an entity in violation of the Stark Law, denial of payment for the services provided in violation of the prohibition, and civil penalties of up to \$15,000 per service arising out of the prohibited referral. Additionally, a person who engages in a scheme to circumvent the Stark Law's prohibition may be subject to a civil penalty of up to \$100,000. A violation of PORA is a misdemeanor and could result in civil penalties and criminal fines.

Other states have self-referral restrictions with which we have to comply that differ from those imposed by federal and California law.

While we have attempted to comply with these laws, it is possible that some of our financial arrangements with pathologists and other physicians could be subject to regulatory scrutiny at some point in the future, and we cannot

provide assurance that we will be found to be in compliance with these laws following any such regulatory review.

Federal, State and Foreign Fraud and Abuse Laws

The federal Anti-Kickback Statute prohibits, among other things, knowingly and willfully offering, paying, soliciting or receiving remuneration to induce or in return for purchasing, leasing, ordering or arranging for the purchase, lease or order of any health care item or service reimbursable under a governmental payor program. The definition of “remuneration” has been broadly interpreted to include anything of value, including gifts, discounts, credit arrangements, payments of cash, waivers of co-payments, ownership interests and providing anything at less than its fair market value. Recognizing that the Anti-Kickback Statute is broad and may technically prohibit many innocuous or beneficial arrangements within the health care industry, the HHS has issued a series of regulatory “safe harbors.” These safe harbor regulations set forth certain provisions, which, if met, will assure health care providers and other parties that they will not be prosecuted under the federal Anti-Kickback Statute. Although full compliance with these provisions ensures against prosecution under the federal Anti-Kickback Statute, the failure of a transaction or arrangement to fit within a specific safe harbor does not necessarily mean that the transaction or arrangement is illegal or that prosecution under the federal Anti-Kickback Statute will be pursued. For further discussion of the impact of federal and state health care fraud and abuse laws and regulations on our business, see the section entitled “Risk Factors — Risks Related to Our Business — We are subject to federal and state health care fraud and abuse laws and regulations and could face substantial penalties if we are unable to, or if a tribunal has determined that we do not fully comply with such laws.”

In addition to the administrative simplification regulations discussed above, HIPAA also created two new federal crimes: health care fraud and false statements relating to health care matters. The health care fraud statute prohibits knowingly and willfully executing a scheme to defraud any health care benefit program, including private payors. A violation of this statute is a felony and may result in fines, imprisonment or exclusion from federal health care programs such as the Medicare and Medicaid programs. The false statements statute prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for health care benefits, items or services. A violation of this statute is a felony and may result in fines, imprisonment or exclusion from federal health care programs.

Finally, another development affecting the health care industry is the increased enforcement of the federal False Claims Act and, in particular, actions brought pursuant to the False Claims Act's "whistleblower" or "qui tam" provisions. The False Claims Act imposes liability on any person or entity that, among other things, knowingly presents, or causes to be presented, a false or fraudulent claim for payment by a federal governmental payor program. The qui tam provisions of the False Claims Act allow a private individual to bring actions on behalf of the federal government alleging that the defendant has defrauded the federal government by submitting a false claim to the federal government and permit such individuals to share in any amounts paid by the entity to the government in fines or settlement. In addition, various states have enacted false claim laws analogous to the federal False Claims Act, many of which apply where a claim is submitted to any third-party payor and not merely to a governmental payor program. When an entity is determined to have violated the False Claims Act, it may be required to pay up to three times the actual damages sustained by the government, plus civil penalties ranging from \$5,500 to \$11,000 for each false claim.

Additionally, in Europe various countries have adopted anti-bribery laws providing for severe consequences, in the form of criminal penalties and/or significant fines, for individuals and/or companies committing a bribery offence. Violations of these anti-bribery laws, or allegations of such violations, could have a negative impact on our business, results of operations and reputation. For instance, in the United Kingdom, under the Bribery Act 2010, which went into effect in July 2011, a bribery occurs when a person offers, gives or promises to give a financial or other advantage to induce or reward another individual to improperly perform certain functions or activities, including any function of a public nature. Bribery of foreign public officials also falls within the scope of the Bribery Act 2010. Under the new regime, an individual found in violation of the Bribery Act 2010, faces imprisonment of up to 10 years. In addition, the individual can be subject to an unlimited fine, as can commercial organizations for failure to prevent bribery.

There are federal and state laws prohibiting fraudulent billing and providing for the recovery of non-fraudulent overpayments, as a large number of laboratories have been forced by the federal and state governments, as well as by private payors, to enter into substantial settlements under these laws. In particular, if an entity is determined to have violated the federal False Claims Act, it may be required to pay up to three times the actual damages sustained by the government, plus civil penalties ranging from \$5,500 to \$11,000 for each separate false claim. While there are many potential bases for liability under the federal False Claims Act, such liability primarily arises when an entity knowingly submits, or causes another to submit, a false claim for reimbursement to the federal government. Submitting a claim with reckless disregard or deliberate ignorance of its validity could result in substantial civil liability. A current trend within the health care industry is the increased use of the federal False Claims Act and, in particular, actions under the False Claims Act's "whistleblower" or "qui tam" provisions to challenge providers and suppliers. Those provisions allow a private individual standing to bring actions on behalf of the government, alleging that the defendant has submitted a fraudulent claim for payment to the federal government. The government may join in the lawsuit, but if the government declines to do so, the individual may choose to pursue the lawsuit alone. The government must be kept apprised of the progress of the lawsuit. Whether or not the federal government intervenes in the case, it will receive the majority of any recovery. In addition, various states have enacted laws modeled after the federal False Claims Act.

Even though we believe we are in material compliance with these laws and regulations, it is possible the government may determine that we are not in compliance, in which case we could be subject to civil and criminal penalties.

The Physician Payment Sunshine Act

The Physician Payment Sunshine Act, or the Sunshine Act, which was enacted as part of the ACA, requires applicable manufacturers of drugs, devices, biologicals, or medical supplies covered under Medicare, Medicaid or the Children's Health Insurance Program, to report annually to HHS payments or other transfers of value made by that entity, or by a third party as directed by that entity, to physicians and teaching hospitals, or to third parties on behalf of physicians or teaching hospitals, during the course of the preceding calendar year. Similar reporting requirements have also been enacted on the state level in the United States, and an increasing number of countries worldwide either have adopted or are considering similar laws requiring transparency of interactions with health care professionals. In addition, some states such as Massachusetts and Vermont impose an outright ban on certain gifts to physicians.

The final rule implementing the Sunshine Act, published on February 8, 2013, requires data collection on payments to begin on August 1, 2013. Failure to comply with the reporting requirements can result in significant civil monetary penalties ranging from \$1,000 to \$10,000 for each payment or other transfer of value that is not reported (up to a maximum per annual report of \$150,000) and from \$10,000 to \$100,000 for each knowing failure to report (up to a maximum per annual report of \$1 million). We believe that our laboratory is not an "applicable manufacturer" as that term is defined in the final rule implementing the Sunshine Act, and, therefore, we are not required to collect data on and report these payments. However, we cannot be certain that regulators will agree with our position. If we are deemed to be an applicable manufacturer subject to the Sunshine Act, we could be subject to civil monetary penalties for failing to comply with the requirements.

These laws could affect our promotional activities by limiting the kinds of interactions we could have with hospitals, physicians or other potential purchasers or users of our tests. Both the disclosure laws and gift bans could impose administrative, cost and compliance burdens on us.

New Medicare Reimbursement Methodology Under PAMA

The Protecting Access to Medicare Act (“PAMA”), which became law on April 1, 2014, significantly reforms the way in which the Medicare program will pay for clinical laboratory services going forward. Under PAMA, starting in 2017, CMS will be required to base its payments to clinical laboratories for diagnostic tests on the amounts that are being paid by commercial health insurance plans for such tests. On October 1, 2015, CMS issued a proposed rule to implement PAMA that would require applicable laboratories to begin reporting the amounts that they are paid for their clinical laboratory tests by private health insurers to CMS, beginning in the first quarter of 2016. Based on the data reported, CMS would, in general, calculate weighted median payments for each test, and use these amounts as new Clinical Laboratory Fee Schedule (“CLFS”) rates beginning in 2017. PAMA provides that, for the first two years, (that is, 2017 through 2019), a payment price cannot be reduced by more than 10 percent per year and thereafter, through 2022, a test payment cannot be reduced by more than 15 percent per year. PAMA authorizes CMS to impose civil monetary penalties of up to \$10,000 per day for each failure to report or each misrepresentation or omission in reporting applicable information to CMS. Because no final rule has yet been published, the ultimate impact of PAMA and its implementing regulations on our business remains unclear.

Food and Drug Administration

The FDA regulates the sale or distribution in interstate commerce, of medical devices, including in vitro diagnostic test kits. The information that must be submitted to the FDA in order to obtain clearance or approval to market a new medical device varies depending on how the medical device is classified by the FDA. Medical devices are classified into one of three classes on the basis of the controls deemed by the FDA to be necessary to reasonably ensure their safety and effectiveness. Class I devices are subject to general controls, including labeling, listing, registration, and reporting. It may also include pre-market notification and adherence to the FDA’s quality system regulation, which are device-specific good manufacturing practices. Class II devices are subject to general controls and special controls, such as performance standards and post-market surveillance. Class III devices are subject to most of the previously identified requirements as well as to PMA. Most in vitro diagnostic kits are regulated as Class I or Class II devices. Entities that fail to comply with FDA requirements can be liable for criminal or civil penalties, recalls, seizures, orders to cease manufacturing and restrictions on labeling and promotion.

The FDA presently requires clearance or approval of diagnostic test kits that are sold to laboratories, hospitals and doctors, considering them to be medical devices. However, diagnostic tests that are developed and performed by a CLIA-certified reference laboratory, known as “home-brew,” “in-house” or LDTs have not been regulated by FDA to date. The FDA has stated that it has the power to regulate LDTs such as the ones that we develop. Nevertheless, it has exercised enforcement discretion and not regulated most LDTs performed by high complexity CLIA certified laboratories. It is possible, perhaps likely, that FDA will decide to more actively regulate LDTs, which could lead to pre-market and post-market obligations. Section 1143 of the Food and Drug Administration Safety and Innovation Act, signed by the President on July 9, 2012, requires FDA to notify Congress at least 60 days prior to issuing a draft or final guidance regulating LDTs and provide details of the anticipated action.

Class II devices are subject to FDA's general controls, and any other special controls as deemed necessary by FDA to provide reasonable assurance of the safety and effectiveness of the device. Pre-market review and clearance by FDA for Class II devices are generally accomplished through the 510(k) pre-market notification procedure. Pre-market notification submissions are subject to user fees, unless a specific exemption applies. To obtain 510(k) clearance for a medical device (or for certain modifications to devices that have received 510(k) clearance), a manufacturer must submit a pre-market notification demonstrating that the proposed device is substantially equivalent to a previously cleared 510(k) device or to a pre-amendment device that was in commercial distribution before May 28, 1976, or a predicate device, for which FDA has not yet called for the submission of a PMA application. In making a determination that the device is substantially equivalent to a predicate device, FDA compares the proposed device to the predicate device or predicate devices and assesses whether the subject device is comparable to the predicate device or predicate devices with respect to intended use, technology, design and other features which could affect the safety and effectiveness. If FDA determines that the subject device is substantially equivalent to the predicate device or predicate devices, the subject device may be cleared for marketing. FDA's 510(k) clearance pathway generally takes from three to twelve months from the date the application is completed, but can take significantly longer. Moreover, in January 2011, FDA announced twenty-five specific action items it intended to take to improve transparency and predictability of the 510(k) program. We anticipate that the changes may also result in additional requirements with which manufacturers will need to comply in order to obtain or maintain 510(k) clearance for their devices. These additional requirements could increase the costs or time for manufacturers' seeking marketing clearances through the 510(k) process. Moreover, the 510(k) process could result in a not-substantially equivalent determination, in which case the device would be regulated as a Class III device, discussed below.

Class III devices are those devices which are deemed by FDA to pose the greatest risk, such as life-sustaining, life-supporting or implantable devices, have a new intended use, or use advanced technology that is not substantially equivalent to that of a legally marketed device. Reasonable assurance of the safety and effectiveness of Class III devices cannot be assured solely by the general controls and the other requirements described above. These devices are required to undergo the PMA process in which the manufacturer must demonstrate reasonable assurance of the safety and effectiveness of the device to FDA's satisfaction. A PMA application must provide extensive preclinical and clinical trial data and also information about the device and its components regarding, among other things, device design, manufacturing and labeling. PMA applications (and supplemental PMA applications) are subject to significantly higher user fees than are 510(k) pre-market notifications. After approval of a PMA, a new PMA or PMA supplement is required in the event of a modification to the device, its labeling or its manufacturing process. The PMA process, including the gathering of clinical and nonclinical data and the submission to and review by FDA, can take several years.

A clinical trial may be required in support of a 510(k) submission and generally is required for a PMA application. These trials generally require an effective Investigational Device Exemption from FDA for a specified number of patients, unless the product is exempt from Investigational Device Exemption requirements or deemed a non-significant risk device eligible for more abbreviated Investigational Device Exemption requirements. The Investigational Device Exemption application must be supported by appropriate data, such as animal and laboratory testing results. Clinical trials may begin 30 days after the submission of the Investigational Device Exemption application unless FDA or the appropriate institutional review boards at the clinical trial sites place the trial on clinical hold.

After a device is placed on the market, regardless of the classification or pre-market pathway, it remains subject to significant regulatory requirements. Even if regulatory approval or clearance of a medical device is granted, FDA may impose limitations or restrictions on the uses and indications for which the device may be labeled and promoted. Medical devices may be marketed only for the uses and indications for which they are cleared or approved. Device manufacturers must also establish registration and device listings with FDA. A medical device manufacturer's manufacturing processes and those of its suppliers are required to comply with the applicable portions of the Quality Systems Regulations, which cover the methods and documentation of the design, testing, production, processes, controls, quality assurance, labeling, packaging and shipping of medical devices. Domestic facility records and manufacturing processes are subject to periodic unscheduled inspections by FDA. FDA also may inspect foreign facilities that export products to the United States.

Failure to comply with applicable regulatory requirements can result in enforcement action by FDA, which may include any of the following sanctions: warning letters, fines, injunctions, civil or criminal penalties, recall or seizure of current or future products, operating restrictions, partial suspension or total shutdown of production, denial of 510(k) clearance or PMA applications for new products, or challenges to existing 510(k) clearances or PMA applications.

If they become regulated by FDA, we believe that our LDTs would likely be regulated as either Class II or Class III devices. It is also possible that some may fall into one Class and some into the other. Accordingly, some level of pre-market review — either a 510(k) or a PMA — would likely be required for each test. While the data requirements are typically greater for Class III devices, the data required for Class II devices has increased, and it is likely that some amount of clinical data (retrospective or prospective or both) would be required for either type of submission. Currently, FDA is undertaking a review of the adequacy of the 510(k) process. It is difficult to predict what changes may result, but it should be assumed that any changes will increase, not decrease, the regulatory requirements.

If the FDA decides to regulate MyPRS® or any future test of ours, it could classify the test as a Class II or Class III device. This would mean that we would have to invest substantial time and resources into obtaining FDA approval and we might have to withdraw the applicable test from the market. This could adversely affect our operations, revenues and our potential to be a profitable or viable entity.

The FDA has stated that it intends to regulate some LDTs as devices. On October 3, 2014, the FDA published a proposed risk-based framework for LDTs, which are tests that are designed, manufactured, and used within a single laboratory. This draft guidance indicates that FDA would like to establish an LDT oversight framework, including premarket review for higher-risk LDTs, such as those that have the same intended use as FDA-approved or cleared companion diagnostics currently on the market. FDA's notice states that FDA does not consider devices to be LDTs if they are designed or manufactured completely, or partly, outside of the laboratory that offers and uses them. The degree to which in-house tests are regulated by the FDA has also been the focus of recent Congressional attention, and Congress is considering the introduction of legislation that would subject at least some such tests to pre-market review or approval by the FDA.

MyPRS[®] and the other tests being developed by the Company include the use of genes and determine whether a patient falls into a high or low risk for disease recurrence or response to a particular chemotherapy. The Company plans to continue to develop and offer these tests as LDTs unless it becomes clearer that these tests are subject to regulation by the FDA. We will continue to monitor both the FDA and Congress and we intend to comply with any new requirements that may apply.

Good Laboratory Practice (“GLP”)

We are subject to various regulatory requirements designed to ensure the quality and integrity of our non-clinical testing processes. Our standard operating procedures are written in accordance with applicable regulations and guidelines for operating in the United States. The industry standards for conducting preclinical laboratory testing are embodied in GLP regulations promulgated by the FDA. In the United States, non-clinical studies intended for FDA submission must be conducted in accordance with GLP regulations; foreign governments may require our North American clients to comply with certain regulatory requirements of other countries (in order to gain approval within these countries), such as regulations promulgated by the Japanese Ministry of Health, Labor and Welfare and Ministry of Agriculture, Forestry and Fisheries, and in Europe, the Organization for Economic Co-operation and Development. GLP regulations specify requirements for facilities, equipment, and professional staff and standardized procedures for conducting studies, including procedures for recording and reporting data and for managing study materials and records. We have established a required quality assurance program that monitors ongoing compliance with GLP regulations by auditing test data and reporting and conducting inspections of testing procedures.

Our business is also subject to regulation under state and federal laws regarding environmental protection and hazardous substances control, such as the Federal Occupational Safety and Health Act, or OSHA, the Environmental Protection Act, and the Toxic Substances Control Act. These regulations, among other things, require work practice controls, protective clothing and equipment, training and other measures designed to minimize exposure to chemicals and transmission of pathogens. We believe that we are in compliance with these and other applicable laws and that the costs of our ongoing compliance will not have a material adverse effect on our business. However, it is possible that the government will find that we are not in compliance with these requirements, which could have an adverse effect on our business and subject us to regulatory sanctions. In addition, statutes and regulations applicable to our business may be adopted which impose substantial costs to assure compliance or otherwise materially adversely affect our operations.

Regulation of Reimbursement and Coverage

Revenues for clinical laboratory testing services come from a variety of sources and depend significantly on the availability of third-party reimbursement, including from the Medicare and Medicaid programs, commercial insurers and managed care organizations. We are currently a Medicare laboratory services provider and intend to become a Medicaid laboratory services provider. We also receive reimbursement from third-party payors for our testing services. As is the case with health care services generally, the majority of payors pay for our testing services at varying levels that may be significantly lower or otherwise differ from our list prices. Obtaining reimbursement from third-party payors is both time consuming and expensive. Payment from third-party payors may not be sufficient to allow us to sell our services on a profitable and competitive basis.

Corporate Practice of Medicine

Numerous states have enacted laws prohibiting business corporations, such as us, from practicing medicine and employing or engaging physicians to practice medicine, generally referred to as the prohibition against the corporate practice of medicine. These laws are designed to prevent interference in the medical decision-making process by anyone who is not a licensed physician. Violation of these laws may result in civil or criminal fines, as well as sanctions imposed against us and/or the professional through licensure proceedings.

Other Regulatory Requirements

Our laboratory is subject to federal, state and local regulations relating to the handling and disposal of regulated medical waste, hazardous waste and biohazardous waste, including chemical, biological agents and compounds, blood and bone marrow samples and other human tissue. Typically, we use outside vendors who are contractually obligated to comply with applicable laws and regulations to dispose of such waste. These vendors are licensed or otherwise qualified to handle and dispose of such waste.

OSHA has established extensive requirements relating to workplace safety for health care employers, including requirements to develop and implement programs to protect workers from exposure to blood-borne pathogens by preventing or minimizing any exposure through needle stick or similar penetrating injuries.

Employees

As of March 15, 2016, we have 32 employees, all of whom are full time employees. None of our employees is represented by a labor union, and we consider our relationship with our employees to be good.

Available Information

We file our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, amendments to those reports, and other information with the U.S. Securities and Exchange Commission (“SEC”). We will supply a copy of any document we file with the SEC, without charge. To request a copy, please contact Investor Relations, Signal Genetics, Inc., 5740 Fleet Street, Carlsbad, CA 92008, USA. The public may also read and copy any document we file with the SEC at its public reference facilities at 100 F Street NE, Washington, D.C. 20549, or by calling the SEC at 1-800-SEC-0330, or by accessing the SEC's website at www.sec.gov, where the SEC maintains reports, proxy and information statements and other information regarding us and other issuers that file electronically with the SEC. In addition, as soon as reasonably practicable after such materials are filed with or furnished to the SEC, we make copies available to the public free of charge through our website at www.signalgenetics.com. We also regularly post on our corporate website copies of our press releases as well as additional information about us.

