

SIGNAL GENETICS LLC
Form 424B4
June 19, 2014

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Registration No. 333-194668

PROSPECTUS

850,000 Shares Common Stock

This is a firm commitment initial public offering of 850,000 shares of common stock by Signal Genetics, Inc. No public market currently exists for our shares.

Our common stock has been approved for listing on The NASDAQ Capital Market under the symbol SGNL.

We are an emerging growth company under applicable Securities and Exchange Commission rules and will be eligible for reduced public company disclosure requirements. See Summary Implications of Being an Emerging Growth Company.

Our business and an investment in our securities involves a high degree of risk. See Risk Factors beginning on page 13 of this prospectus for a discussion of information that you should consider before investing in our securities.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

	Per Share	Total
Public offering price	\$ 10.00	\$ 8,500,000
Underwriting discounts and commissions ⁽¹⁾	\$ 0.70	\$ 595,000
Proceeds, before expenses, to us	\$ 9.30	\$ 7,905,000

The underwriters will receive compensation in addition to the underwriting discount. The registration statement, of which this prospectus is a part, also registers for sale warrants to purchase 42,500 shares of our common stock to be issued to the representative of the underwriters. We have agreed to issue the warrants to the representative of the underwriters as a portion of the underwriting compensation payable to the underwriters in connection with this offering. See Underwriting beginning on page 115 of this prospectus for a description of compensation payable to the underwriters, including a description of the warrants.

We have granted a 45-day option to the underwriters to purchase up to 127,500 additional shares of common stock solely to cover over-allotments, if any.

The underwriters expect to deliver the shares against payment therefor on or about June 23, 2014.

Aegis Capital Corp

June 17, 2014

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You should rely only on the information contained in this prospectus or in any free writing prospectus that we may specifically authorize to be delivered or made available to you. We have not, and the underwriters have not, authorized anyone to provide you with any information other than that contained in this prospectus or in any free writing prospectus we may authorize to be delivered or made available to you. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. This prospectus may only be used where it is legal to offer and sell our securities. The information in this prospectus is accurate only as of the date of this prospectus, regardless of the time of delivery of this prospectus or any sale of our securities. Our business, financial condition, results of operations and prospects may have changed since that date. We are not, and the underwriters are not, making an offer of these securities in any jurisdiction where the offer is not permitted.

For investors outside the United States: We have not and the underwriters have not done anything that would permit this offering or possession or distribution of this prospectus in any jurisdiction where action for that purpose is required, other than in the United States. Persons outside

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the United States who come into possession of this prospectus must inform themselves about, and observe any restrictions relating to, the offering of securities and the distribution of this prospectus outside the United States.

This prospectus includes statistical and other industry and market data that we obtained from industry publications and research, surveys and studies conducted by third parties. Industry publications and third-party research, surveys and studies generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. We believe that the data obtained from these industry publications and third-party research, surveys and studies are reliable. The Company is ultimately responsible for all disclosure included in this prospectus.

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PROSPECTUS SUMMARY

This summary highlights information contained elsewhere in this prospectus and does not contain all of the information that you should consider in making your investment decision. Before investing in our securities, you should carefully read this entire prospectus, including our financial statements and the related notes and the information set forth under the headings Risk Factors and Management's Discussion and Analysis of Financial Condition and Results of Operations in each case included elsewhere in this prospectus. In this prospectus, unless the context otherwise requires, the terms we, us, our, Signal Genetics and Company refer to Signal Genetics LLC and its consolidated subsidiaries for the periods prior to the consummation of the corporate conversion (as described below), and such terms refer to Signal Genetics, Inc. and its consolidated subsidiaries for the periods after the consummation of the corporate conversion. Except as disclosed in the prospectus, the consolidated financial statements and selected historical consolidated financial data and other financial information included in this registration statement are those of Signal Genetics LLC and its subsidiaries and do not give effect to the corporate conversion. We have provided definitions for some of the terms we use to describe our business and industry and other terms used in this prospectus in the Glossary of Terms beginning on page 124 of this prospectus.

Immediately prior to the effectiveness of the registration statement of which this prospectus is a part, we have completed a number of transactions pursuant to which Signal Genetics, Inc. has succeeded to the business of Signal Genetics LLC and its consolidated subsidiaries and the members of Signal Genetics LLC have become stockholders of Signal Genetics, Inc. In this prospectus, we refer to such transactions as the corporate conversion.

Signal Genetics, Inc.

Business Overview

We are an emerging commercial stage, molecular 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. We were founded in January 2010 and became the exclusive licensee in our licensed field to the renowned research on multiple myeloma performed at the University of Arkansas for Medical Sciences, or UAMS, in April 2010.

Multiple myeloma, or 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 immunoglobins, 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, or M protein. The hallmark characteristic of myeloma 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 leukemia and represents approximately 15% of all hematological malignancies. According to the American Cancer Society, or ACS, approximately 22,350 new cases of MM are expected to be diagnosed in the United States in 2013 and approximately 10,710 deaths from MM are expected to occur in the United States in 2013. More Americans will die from MM this year 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 77,617 people currently living with MM in the United States. The five-year survival rate for people with MM is about 43%. The ACS estimates that the lifetime risk in the United States of getting MM is 1 in 149.

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

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staging. Staging is the process of determining how widespread or advanced the cancer is. Under the International Staging System, or 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 determination of the course of treatment for a patient and that patient's outlook or prognosis for recovery. 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 myeloma, including when treatment should begin and what treatments to use, based upon a patient's individual risk for relapse. However, those experts caring for MM patients have been faced with a staging system that predates the current era and a large amount of new genomic information that could assist in the staging process. The traditional approach which utilizes cytogenetic techniques, such as karyotyping and fluorescent in-situ hybridization, or FISH, for staging has not been able to accurately stage MM patients or fully assess the risk of relapse and classify MM. A more comprehensive and systematic approach is necessary to meet this unmet medical need.

Our flagship diagnostic service is the Myeloma Prognostic Risk Signature, or MyPRS®. The MyPRS® test is a microarray-based gene expression profile, or GEP, assay that tests for presence of specific groups of genes that can predict low or high level risk of early relapse. The MyPRS® test provides a whole-genomic expression profile of a person's myeloma. 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 can help make personalized treatment possible, and our MyPRS® test is the first one to be developed for multiple myeloma according to the 2007 John Shaughnessy paper in the Journal Blood. MyPRS® can be used at the time of initial myeloma diagnosis or when the patient has experienced a relapse to aid physicians in selecting the optimal treatment regime for each patient's unique condition. Specifically, the test helps allow:

risk stratification to help distinguish patients with indolent myeloma 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 myeloma sub classification that may affect the specific choice of therapies.

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 has been certified under the Clinical Laboratory Improvement Amendments of 1988, or CLIA, to perform high complexity testing. We are either licensed, or not subject to licensure, and can thus perform our test using specimens collected in 49 of the 50 states. We are currently seeking a license in New York for the MyPRS® test, which would enable us to perform MyPRS® testing for patients located in New York. 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 asymptomatic monoclonal gammopathies, or AMG, the precursor conditions to MM. There is, however, currently no projected timeline for our use of MyPRS® in AMG patients. For a discussion of MyPRS® in AMG patients see [Market Opportunity](#), 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). We also plan to launch a

targeted next generation gene sequencing service to assist our physician customers in further characterizing their MM patients and assisting with identifying the potential to use targeted therapies based upon the specific genetic mutations of their patients' tumors. It is our intent to add such complementary services to our proprietary MyPRS® franchise to provide a more comprehensive suite of tests for our oncologist customers and their patients.

Market Opportunity

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,

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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, and in other cases can be indolent. Unfortunately, identifying those patients who will likely die of something other than their particular cancer diagnosis 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, their use has not resulted in uniformly better outcomes, such as overall survival. In part, this is because MM is a disease with significant tumor heterogeneity at the molecular level. Specialists in MM have long recognized the need for diagnostic tests that accurately identify the mutations and genotype of each patient with MM in order to allow risk stratification, predict prognosis and response to treatment. 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 have used plasma cell labeling indices, chemical markers, imaging studies and genetic abnormalities at the chromosomal level (*e.g.*, cytogenetics) to improve their ability to 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.

Unlike many forms of cancer, multiple myeloma is often asymptomatic, even in advanced stages. MM begins as a precursor condition known as monoclonal gammopathy of undetermined significance, or 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 develop MM.

Aside from the precursor condition MGUS, MM exists on a spectrum from asymptomatic or smoldering multiple myeloma, or AMM, to full-blown MM. Collectively, these precursor conditions, MGUS and AMM 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 impact on survival time.

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 at approximately 33,500 patients per year, including

newly diagnosed and relapsed patients. We believe we currently service just over 2% of this market. We estimate that the addition of an AMG progression indication feature for the MyPRS® test could expand the MyPRS® addressable market to more than 130,000 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.

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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 an accuracy of up to 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.

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 for Research and Therapy, or MIRT, in our licensed field. MIRT 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 MIRT. A number of treatment improvements for myeloma patients were first discovered at MIRT. The physicians at MIRT 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.

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

We currently license, or own outright, ten (10) issued patents and twenty-six (26) 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 four 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

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classification for multiple myeloma using RNA from plasma cells, methods of identifying groups of genes that can distinguish normal and multiple myeloma plasma cells by isolating RNA from CD138 positive plasma cells and identifying differentially expressed genes, methods of diagnosing multiple myeloma by examining mRNA levels or chromosomal translocations of particular genes from plasma cells, and methods of determining the prognosis of a multiple myeloma 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 several pending patent applications in the U.S. and abroad directed to other aspects of the MyPRS® test. For example, one U.S. application, along with Canadian and European counterpart applications, describes 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 fully 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 sales person is well versed in the science and technology behind our MyPRS® test. We will continue to grow our sales force 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, or LCD, in March 2011 from the Arkansas Medicare Administrative Contractor, or MAC, which at the time was Pinnacle Medical Services for MyPRS®. 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 with additional hiring of managed care professionals, we will be able to achieve positive coverage determinations from a majority of the major third-party payors in the United States. However, those efforts may take quite some time and may not be successful.

Experienced oncology-centered laboratory and clinical trial services

Our specimens are tested and interpreted by highly qualified oncology-focused laboratory professionals with more than 56 years of cumulative experience with gene expression-based diagnostic testing technology. Because our

clinical staff is highly specialized in oncology, 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 sales force which currently consists of one employee;

Broadening the base of healthcare insurance companies that have approved reimbursements for MyPRS®

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Expanding the diagnostic indications for MyPRS® to include AMG, the precursor condition to MM;
Establishing partnerships with other reference laboratories to expand the market reach for MyPRS®;
Pursuing 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 conventional tests used by physicians who care for MM patients;
Pursuing additional collaborations 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.

Risks

Our business and our ability to execute our business strategy are subject to a number of risks of which you should be aware before you decide to buy our common stock. In particular, you should carefully consider the following risks, which are discussed more fully in **Risk Factors** beginning on page 13 of this prospectus.

We are an early stage company with a limited commercial history and a history of net losses; we expect to incur net losses in the future, and we may never achieve sustained profitability.

We may need to raise additional financing to meet our liquidity requirements.

If our CLIA certificate or any other required license or certification is lost, suspended or restricted, we may not be able to perform or get paid for any lab tests, temporarily or permanently.

A small number of test ordering sites account for most of the sales of our tests and services. If any of these sites orders fewer tests from us for any reason, our revenues could decline.

Our business depends on our ability to successfully develop and commercialize novel cancer diagnostic tests and services, which is time consuming and complex, and our development efforts may fail.

If we are unable to obtain regulatory clearance or approvals in the United States or if we experience delays in receiving clearance or approvals, our growth strategy may not be successful and our business may not be viable.

If we are unable to execute our marketing strategy for our cancer diagnostic tests and are unable to gain acceptance in the market, we may be unable to generate sufficient revenue to sustain our business.

We rely on a limited number of third parties for manufacture and supply of all of our laboratory instruments, tests and materials, and we may not be able to find replacement suppliers or manufacturers in a timely manner in the event of any disruption, which could adversely affect our business.

If our sole laboratory facility becomes damaged or inoperable, or we are required to vacate the facility, our ability to provide services and pursue our research and development efforts may be jeopardized.

We expect to continue to incur significant expenses to develop and market our diagnostic tests, which could make it difficult for us to achieve and sustain profitability.

If pathologists and oncologists decide not to order our diagnostic tests, we may be unable to generate sufficient revenue to sustain our business.

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We depend on certain collaborations with third parties for the supply of certain tissue samples and biological materials that we use in our research and development efforts. If the costs of such collaborations increase after we complete our initial public offering or our third-party collaborators terminate their relationship with us, our business may be materially harmed.

Our inability to attract, hire and retain a sufficient number of qualified sales professionals would hamper our ability to increase demand for our tests, to expand geographically and to successfully commercialize any other diagnostic tests or services we may develop.

We outsource our billing and collections to a third-party provider. Our provider may fail in its duties to us and thereby reduce our cash collections and harm our business.

Health care policy changes, including recently enacted legislation reforming the U.S. health care system, may have a material adverse effect on our financial condition, results of operations and cash flows.

Our commercial success could be compromised if third-party payors, including managed care organizations and Medicare, do not provide coverage and reimbursement, breach, rescind or modify their contracts or reimbursement policies or delay payments for our molecular diagnostic tests.

We depend on Medicare and a limited number of private payors for a significant portion of our revenues and if these or other payors stop providing reimbursement or decrease the amount of reimbursement for our tests, our revenues could decline.

If the U.S. Food and Drug Administration, or FDA, were to begin requiring approval or clearance of our tests, we could incur substantial costs and time delays associated with meeting requirements for pre-market clearance or approval or we could experience decreased demand for, or reimbursement of, our tests.

If we were required to conduct additional clinical trials prior to continuing to offer our proprietary MyPRS® test or any other tests that we may develop as Laboratory Developed Tests, or LDTs, those trials could lead to delays or failure to obtain necessary regulatory approval, which could cause significant delays in commercializing any future tests and harm our ability to achieve sustained profitability.

If we are unable to maintain intellectual property protection, our competitive position could be harmed.

Our rights to use technologies licensed from third parties are not fully within our control, and we may not be able to sell our diagnostic tests and other services if we lose our existing rights or cannot obtain new rights on reasonable terms.

Our inability to meet the continued listing requirements of The NASDAQ Capital Market could result in a delisting of our common stock and have a negative effect on the price of our common stock, which could impair your ability to sell or purchase our common stock when you wish to do so.

Our independent registered public accounting firm has expressed substantial doubt about our ability to continue as a going concern.

We have identified a material weakness in our internal control over financial reporting. If our internal control over financial reporting is not effective, we may not be able to accurately report our financial results or file our periodic reports in a timely manner, which may cause investors to lose confidence in our reported financial information and may lead to a decline in our stock price.

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Implications of Being an Emerging Growth Company

As a company with less than \$1.0 billion in revenue during our last fiscal year, we qualify as an emerging growth company as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. For so long as we remain an emerging growth company, we are permitted and intend to rely on exemptions from specified disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include:

being permitted to provide only two years of audited financial statements, in addition to any required unaudited interim financial statements, with correspondingly reduced Management's Discussion and Analysis of Financial Condition and Results of Operations disclosure;

not being required to comply with the auditor attestation requirements in the assessment of our internal control over financial reporting;

not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements;

reduced disclosure obligations regarding executive compensation; and

exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved.

We may take advantage of these provisions for up to five years or such earlier time that we are no longer an emerging growth company. We would cease to be an emerging growth company if we have more than \$1.0 billion in annual revenues, have more than \$700.0 million in market value of our capital stock held by non-affiliates or issue more than \$1.0 billion of non-convertible debt over a three-year period. We may choose to take advantage of some, but not all, of the available exemptions. We have taken advantage of some reduced reporting burdens in this prospectus.

Accordingly, the information contained herein may be different than the information you receive from other public companies in which you hold stock.

In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This provision allows an emerging growth company to delay the adoption of some accounting standards until those standards would otherwise apply to private companies.

We have elected to avail ourselves of this extended transition period for adopting new or revised accounting standards. As a result of this election, our financial statements may not be comparable to companies that comply with public company effective dates.

Corporate Information

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. In connection with the corporate conversion and this offering, Myeloma Health LLC has become a wholly-owned subsidiary of the Company. In connection with this offering, Signal Genetics LLC converted from a Delaware limited liability company to a Delaware corporation. We refer to this as the corporate conversion. In connection with the corporate conversion, each unit of Signal Genetics LLC was converted into shares 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

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business of Signal Genetics LLC and its consolidated subsidiaries. See Corporate Conversion for further information regarding the corporate conversion.

Our principal executive offices are located at 667 Madison Avenue, 14th Floor, New York, New York 10065, and our telephone number is (212) 486-0040. We currently intend to relocate our principal executive offices to the County of San Diego, California upon completion of this offering. Our website address is *www.signalgenetics.com*. Information contained in our website does not form part of the prospectus and is intended for informational purposes only.

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THE OFFERING

Issuer

Signal Genetics, Inc.

Common stock offered by us

850,000 shares (or 977,500 shares if the underwriters exercise their over-allotment option in full).

Over-allotment option

The underwriters have an option for a period of 45 days to purchase up to 127,500 additional shares of our common stock to cover over-allotments, if any.

Common stock to be outstanding immediately after this offering

3,782,629 shares. If the underwriters' over-allotment option is exercised in full, the total number of shares of common stock outstanding immediately after this offering would be 3,910,129.

Use of Proceeds

We intend to use the net proceeds received from this offering to fund continued clinical development of AMG indication for our MyPRS® test and for expansion of our commercial organization, the establishment of our San Diego corporate headquarters, the hiring of an executive team to manage and grow our business, including a Chief Financial Officer with public company experience and a Chief Commercial Officer, the repayment of funds advanced to us by Mr. LeBow to pay certain offering expenses, working capital and general corporate purposes. Pending our use of the net proceeds from this offering, we intend to invest the net proceeds in a variety of capital preservation investments, including short-term, investment grade, interest bearing instruments and U.S. government securities. See Use of Proceeds on page 46.

Representative's warrants

The registration statement of which this prospectus is a part also registers for sale warrants to purchase 42,500 shares of our common stock to the representative of the underwriters as a portion of the underwriting compensation payable to the underwriters in connection with this offering. The warrants will be exercisable for a four-year period commencing one year following the closing of this offering at an exercise price equal to 125% of the initial public offering price of the common stock. Please see Underwriting Representative's Warrants for a description of these warrants.

Risk Factors

See Risk Factors beginning on page 13 and the other information included in this prospectus for a discussion of factors you should carefully consider before investing in our securities.

Proposed symbol and listing

Our common stock has been approved for listing on The NASDAQ Capital Market under the symbol SGNL. Unless we indicate otherwise, the number of shares of our common stock outstanding after this offering is based on the following:

the conversion of approximately \$27.3 million of debt (including principal and interest as of the date of this prospectus), which includes \$20.3 million of debt which is owed to certain entities controlled by Bennett S. LeBow, or LeBow Alpha, the Chairman of our board of directors, into an aggregate of 2,732,629 Class C units, or the debt conversion;

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the consummation of the corporate conversion, pursuant to which all of the outstanding Class A and Class C units of Signal Genetics LLC were converted into an aggregate of 2,932,629 shares of our common stock (2,232,629 of which were issued to LeBow Alpha);

831,593 shares of our common stock reserved for issuance upon the vesting of certain restricted stock unit awards issued to certain employees of the Company immediately prior to this offering (including 277,860 restricted stock units, which are currently vested, but the common stock will not be issued until January 1, 2015); and excludes an additional 413,806 shares of our common stock reserved for future issuance under the new equity incentive plan we intend to adopt immediately prior to this offering.

Unless specifically stated otherwise, the information in this prospectus:

assumes completion of the corporate conversion and debt conversion;

assumes no exercise by the underwriters of their option to purchase up to an additional 127,500 shares of common stock to cover over-allotments, if any;

assumes no exercise of the warrants granted to Aegis Capital Corp. upon completion of this offering;

is based on the initial public offering price of \$10.00 per share; and

assumes that the restricted stock unit awards, which may be settled in cash or stock in the board of directors sole discretion, will be settled solely in stock.

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SUMMARY HISTORICAL CONSOLIDATED FINANCIAL DATA

The following table sets forth our summary statement of operations data for the fiscal years ended December 31, 2012 and 2013 derived from our audited consolidated financial statements and related notes included elsewhere in this prospectus. The summary consolidated financial data for the year ended December 31, 2011 is derived from our audited consolidated financial statements not contained herein. The summary consolidated financial data for the three months ended March 31, 2014 and 2013, and as of March 31, 2014, are derived from our unaudited consolidated financial statements appearing elsewhere in this prospectus and are not necessarily indicative of results to be expected for the full year. Our financial statements are prepared and presented in accordance with generally accepted accounting principles in the United States. The results indicated below are not necessarily indicative of our future performance. You should read this information together with the sections entitled Capitalization, Management's Discussion and Analysis of Financial Condition and Results of Operations and our consolidated financial statements and related notes included elsewhere in this prospectus.

	Three Months Ended		Year Ended		
	March 31,		December 31,		
	2014	2013	2013	2012	2011
Statement of Operations Data:					
Net revenue	\$1,090,923	\$1,139,388	\$4,316,484	\$4,406,042	\$1,915,627
Operating expenses:					
Cost of revenue	663,514	668,967	2,498,940	3,042,184	2,472,390
Selling and marketing	73,070	86,100	378,769	1,325,245	530,876
General and administrative	512,325	417,830	1,788,141	2,907,947	2,589,787
Research and development	8,707	45,743	96,847	225,378	103,317
Lease abandonment				932,287	
Gain on legal settlement			(250,000)		
Total operating expenses	1,257,616	1,218,640	4,512,697	8,433,041	5,696,370
Operating loss	(166,693)	(79,252)	(196,213)	(4,026,999)	(3,780,743)
Interest expense	(539,086)	(457,904)	(1,963,456)	(1,591,341)	(561,029)
Loss from continuing operations	(705,779)	(537,156)	(2,159,669)	(5,618,340)	(4,341,772)
Net loss from discontinued operations, net of tax benefit of \$0				(1,592,945)	(8,492,722)
Net loss	(705,779)	(537,156)	(2,159,669)	(7,211,285)	(12,834,494)
Dividend to member unit holder of Myeloma Health LLC		(90,000)	(285,000)	(390,000)	(140,000)
Net loss attributable to member of Signal Genetics LLC	\$(705,779)	\$(627,156)	\$(2,444,669)	\$(7,601,285)	\$(12,974,494)

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Basic and diluted net loss per unit	\$(7.83)	\$(27.20)
Average units outstanding basic and diluted	90,131	89,891
Pro forma basic and diluted net loss per share ⁽¹⁾	\$(0.25)	\$(0.88)
Pro forma average shares outstanding basic and diluted ⁽¹⁾	2,821,826	2,791,354

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	As of March 31, 2014		
	Actual	Pro Forma ⁽¹⁾	Pro Forma, As Adjusted ⁽²⁾
Balance Sheet Data:			
Cash and cash equivalents	\$ 105,105	\$ 105,105	\$ 7,275,105
Total assets	3,495,332	3,495,332	9,683,197
Total liabilities	28,088,146	1,869,889	887,754
Total members deficiency/stockholders equity	(24,592,814)	1,625,443	8,795,443

	As of December 31, 2013		
	Actual	Pro Forma ⁽¹⁾	Pro Forma, As Adjusted ⁽²⁾
Balance Sheet Data:			
Cash and cash equivalents	\$ 209,348	\$ 209,348	\$ 7,479,348
Total assets	3,672,626	3,672,626	10,287,608
Total liabilities	27,559,661	1,646,125	991,107
Total members deficiency/stockholders equity	(23,887,035)	2,026,501	9,296,501

(1) The pro forma gives effect to (i) the debt conversion (based on the debt outstanding as of March 31, 2014 and as of December 31, 2013, respectively) and (ii) the corporate conversion. Common stock with respect to the vested portion of the restricted stock unit awards will not be issued until January 1, 2015 and is therefore not considered outstanding.

(2) The pro forma, as adjusted balance sheet data reflects the items described in footnote (1) above and gives effect to (i) the conversion of \$1,125,895 of additional debt incurred between March 31, 2014 and the date of this prospectus for March 31, 2014 and \$1,757,733 of additional debt incurred between January 1, 2014 and the date of this prospectus for December 31, 2013 and (ii) our receipt of estimated net proceeds from the sale of 850,000 shares of common stock that we are offering at the initial public offering price of \$10.00 per share, after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

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RISK FACTORS

Any investment in our securities involves a high degree of risk. Investors should carefully consider the risks described below and all of the information contained in this prospectus before deciding whether to purchase our common stock. Our business, financial condition or results of operations could be materially adversely affected by these risks if any of them actually occur. This prospectus also contains forward-looking statements that involve risks and uncertainties. Our actual results could differ materially from those anticipated in these forward-looking statements as a result of certain factors, including the risks we face as described below and elsewhere in this prospectus.

Risks Related to our Financial Condition

We are an early stage company with a limited commercial history and a history of net losses; we expect to incur net losses in the future, and we may never achieve sustained profitability.

We have a limited commercial history. Substantially all of our revenue has been derived from our MyPRS® testing services, which were launched in 2011. We have historically incurred substantial net losses. We incurred losses attributable to a member of Signal Genetics LLC of \$0.7 million, \$2.4 million and \$7.6 million for the three months ended March 31, 2014 and the fiscal years ended December 31, 2013 and 2012, respectively. From our inception in April 2010 through March 31, 2014, we had a members' deficiency of \$24.6 million. Losses are continuing through the date of this prospectus. We expect our losses to continue as a result of ongoing research and development expenses