VERMILLION, INC.
Form S-3
September 15, 2014
As filed with the Securities and Exchange Commission on September 12, 2014

Registration No. 333-[ ]

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM S-3

REGISTRATION STATEMENT

Under

The Securities Act of 1933

Vermillion, Inc.

(Exact Name of Registrant as Specified in its Charter)

Delaware	33-0595156
(State or Other Jurisdiction of Incorporation or Organization)	(I.R.S. Employer Identification Number)

12117 Bee Caves Road, Building Three, Suite 100

Austin, Texas 78738

(512) 519-0400

(Address, Including Zip Code, and Telephone Number,

Including Area Code, of Registrant's Principal Executive Offices)

James LaFrance
President and Chief Executive Officer
12117 Bee Caves Road, Building Three, Suite 100
Austin, Texas 78738
(512) 519-0400
(Name, Address, Including Zip Code, and Telephone Number, Including Area Code, of Agent For Service)

Copies to:

Beth Flaming

John Sabl
Sidley Austin LLP
One South Dearborn Street
Chicago, IL 60603
(312) 853-7000

Approximate date of commencement of proposed sale to the public: From time to time on or after the effective date of this registration statement.

If only securities being registered on this Form are being offered pursuant to dividend or interest reinvestment plans, please check the following box.

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, other than securities offered only in connection with dividend or interest reinvestment plans, check the following box.

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this Form is a registration statement pursuant to General Instruction I.D. or a post-effective amendment thereto that shall become effective upon filing with the Commission pursuant to Rule 462(e) under the Securities Act, check the following box.

If this Form is a post-effective amendment to a registration statement filed pursuant to General Instruction I.D. filed to register additional securities or additional classes of securities pursuant to Rule 413(b) under the Securities Act, check the following box.

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See the definitions of “large accelerated filer,” “accelerated filer” and “smaller reporting company” in Rule 12b-2 of the Exchange Act.

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

CALCULATION OF REGISTRATION FEE

Title of Each Class of Securities to be Registered	Amount to be Registered	Proposed Maximum Offering Price Per Security	Proposed Maximum Aggregate Offering Price	Amount of Registration Fee
Common Stock, par value $0.001 per share	(1)	(2)	(3)	--
Preferred Stock, par value $0.001 per share	(1)	(2)	(3)	--
Warrants (4)	(1)	(2)	(3)	--
Rights (5)	(1)	(2)	(3)	--
Units (6)	(1)	(2)	(3)	--
Total			$50,000,000	$6,440 (7)

(1)Not specified with respect to each class of securities to be registered pursuant to General Instruction II.D. of Form S-3 under the Securities Act of 1933, as amended (the "Securities Act"). This registration statement covers such indeterminate number of shares of common stock, preferred stock, warrants, rights and units as may be issued by the registrant at indeterminate prices, but with an aggregate initial offering price not to exceed $50,000,000. The securities registered hereunder are to be issued or sold from time to time and at prices to be determined. The securities registered hereunder also include securities that may be purchased by underwriters to cover over-allotments, if any. Pursuant to Rule 416 under the Securities Act, this registration statement also includes such additional number of securities in exercise, conversion or exchange of other securities or that may become issuable as a result of any stock splits, stock dividends or similar transactions relating to the securities issued hereunder.

(2)As permitted pursuant to Note 2 of Notes to the "Calculation of Registration Fee" Table of Form S-3, this information is omitted because the filing fee is calculated pursuant to Rule 457(o) under the Securities Act.

(3)Estimated solely for purposes of calculating the registration fee in accordance with Rule 457(o) under the Securities Act.

(4)Warrants may be sold separately or together with any of the securities registered hereby and may be exercisable for preferred stock or common stock registered hereby. Because the warrants will provide a right only to purchase such securities offered hereunder, no additional registration fee is required.

(5)Rights will represent rights to purchase shares of common stock or shares of preferred stock registered hereby. Because the rights will provide a right only to purchase such securities offered hereunder, no additional registration fee is required.

(6)Each unit will be issued under a unit agreement and will represent an interest in two or more securities registered hereby, which may or may not be separable.

(7)Calculated pursuant to Rule 457(o) under the Securities Act.

THE REGISTRANT HEREBY AMENDS THIS REGISTRATION STATEMENT ON SUCH DATE OR DATES AS MAY BE NECESSARY TO DELAY ITS EFFECTIVE DATE UNTIL THE REGISTRANT SHALL FILE A FURTHER AMENDMENT WHICH SPECIFICALLY STATES THAT THIS REGISTRATION STATEMENT SHALL THEREAFTER BECOME EFFECTIVE IN ACCORDANCE WITH SECTION 8(a) OF THE SECURITIES ACT OR UNTIL THE REGISTRATION STATEMENT SHALL BECOME EFFECTIVE ON SUCH DATE AS THE SECURITIES AND EXCHANGE COMMISSION, ACTING PURSUANT TO SAID SECTION 8(a), MAY DETERMINE.

EXPLANATORY NOTE

This registration statement contains two prospectuses:

- a base prospectus which covers the offer, issuance and sale of up to $50,000,000 of our common stock, preferred stock, warrants, rights and units; and

- an at-the-market offering prospectus covering the offer, issuance and sale of up to $15,000,000 of our common stock pursuant to a sales agreement with Cantor Fitzgerald & Co.

The base prospectus immediately follows this explanatory note. The at-the-market offering prospectus immediately follows the base prospectus. Upon termination of the sale agreement with Cantor Fitzgerald & Co., any portion of the $15,000,000 included in the at-the-market offering prospectus that is not sold pursuant to the sales agreement will be available for sale in other offerings pursuant to the base prospectus, and if no shares are sold under the sales agreement, the full $50,000,000 of securities may be sold in other offerings pursuant to the base prospectus and a corresponding prospectus supplement.

The information in this prospectus is not complete and may be changed. We may not sell these securities until the Registration Statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities and it is not soliciting an offer to buy these securities in any state where the offer or sale is not permitted.

Subject to completion, dated SEPTEMBER 12, 2014

PROSPECTUS

$50,000,000 Aggregate Offering Price of

Common Stock, Preferred Stock, Warrants, Rights and Units

Vermillion, Inc., a Delaware corporation ("Vermillion"), may offer and sell from time to time, in one or more offerings, common stock, preferred stock, warrants, rights and units for an aggregate initial offering price up to $50,000,000 in amounts, at prices and on terms that Vermillion will determine at the time of the offering.

This prospectus describes general terms that apply to these securities. When we decide to sell a particular class or series of those securities, we will provide specific terms of the securities, including the initial offering price and the aggregate amount of the offering, in one or more supplements to this prospectus. Any prospectus supplement may also add, update, or change information contained in this prospectus. You should carefully read this prospectus and the applicable prospectus supplement, as well as the documents incorporated or deemed to be incorporated by reference in this prospectus before you invest in our securities.

These securities may be offered and sold in the same offering or in separate offerings; to or through underwriters, dealers, and agents; or directly to purchasers. The names of any underwriters, dealers, or agents involved in the sale of our securities, their compensation and any over-allotment options held by them will be described in the applicable prospectus supplement. For a more complete description of the plan of distribution of these securities, see the section entitled "Plan of Distribution" beginning on page 8 of this prospectus.

Our common stock is traded on The NASDAQ Capital Market under the symbol "VRML". On September 11, 2014, the last reported sale price for our common stock on The NASDAQ Capital Market was $2.21 per share. As of September 12, 2014, the aggregate market value of our outstanding common stock held by our non-affiliates, as calculated pursuant to the rules of the Securities and Exchange Commission, was $47,592,445. Pursuant to General Instruction I.B.6 of Form S-3, in no event will we sell securities in a public primary offering with a value exceeding more than one-third of our "public float" (the market value of our common stock held by our non-affiliates) in any 12-month period so long as our public float remains below $75,000,000. We have not sold any of our common stock or securities convertible into our common stock during the 12 calendar months prior to and including the date of this prospectus.

INVESTING IN OUR SECURITIES INVOLVES SUBSTANTIAL RISKS. YOU SHOULD CONSIDER THE "RISK FACTORS" BEGINNING ON PAGE 5 OF THIS PROSPECTUS, IN THE DOCUMENTS THAT ARE

INCORPORATED BY REFERENCE INTO THIS PROSPECTUS AND, IF APPLICABLE, IN RISK FACTORS DESCRIBED IN ANY ACCOMPANYING PROSPECTUS SUPPLEMENT BEFORE BUYING ANY OF OUR SECURITIES.

NEITHER THE SECURITIES AND EXCHANGE COMMISSION NOR ANY STATE SECURITIES COMMISSION HAS APPROVED OR DISAPPROVED OF THESE SECURITIES OR PASSED UPON THE ADEQUACY OR ACCURACY OF THIS PROSPECTUS. ANY REPRESENTATION TO THE CONTRARY IS A CRIMINAL OFFENSE.

The date of this prospectus is , 2014.

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement on Form S-3 that we filed with the Securities and Exchange Commission, or the SEC, on September 12, 2014, using a “shelf” registration process. Under this shelf registration process, we may, from time to time, sell any combination of the securities described in this prospectus in one or more offerings up to the aggregate amount of $50,000,000.

This prospectus provides you with a general description of the securities we may offer. The prospectus supplement may add to, update or change information contained in this prospectus, and, accordingly, to the extent inconsistent, information in this prospectus is superseded by the information in the prospectus supplement.

The prospectus supplement may describe, as applicable: the terms of the securities offered; the initial public offering price; the price paid for the securities; net proceeds; and the other specific terms related to the offering of the securities.

You should rely only on the information that we have provided or incorporated by reference in this prospectus, any applicable prospectus supplement and any related free writing prospectus that we may authorize to be provided to you. We have not authorized anyone to provide you with different information. No dealer, salesperson or other person is authorized to give any information or to represent anything not contained in this prospectus or any applicable prospectus supplement or any related free writing prospectus that we may authorize to be provided to you. If anyone provides you with different or inconsistent information, you should not rely on it. You should assume that the information in this prospectus, any applicable prospectus supplement or any related free writing prospectus is accurate only as of the date on the cover of the document and that any information we have incorporated by reference is accurate only as of the date of the document incorporated by reference, regardless of the time of delivery of this prospectus, any applicable prospectus supplement or any related free writing prospectus, or any sale of a security. Our business, financial condition, results of operations and prospects may have changed since those dates.

SUMMARY

This summary highlights certain information contained in greater detail elsewhere in this prospectus or incorporated by reference into this prospectus. This summary is not complete and does not contain all of the information that you should consider before deciding whether to invest in our securities. You should carefully read this prospectus, any accompanying prospectus supplements, any related free writing prospectus that we have authorized for use in connection with this offering and the documents incorporated by reference herein and in any accompanying prospectus supplement, including the information referred to under the heading "Risk Factors" in this prospectus on page 5, under the heading "Risk Factors" contained in the applicable prospectus supplement and in the documents incorporated by reference into this prospectus and any prospectus supplement. Unless the context requires otherwise, all references in this prospectus to "Vermillion," "the company," "we," "us," "our" or similar references mean Vermillion, Inc. together with its consolidated subsidiaries.

Our Company

Our vision is to drive advancement in personalized medical management — initially focused on ovarian health — to improve outcomes for patients, physicians and providers.

We are dedicated to the discovery, development and commercialization of novel high-value diagnostic tests that help physicians diagnose, treat and improve outcomes for patients. Our tests are intended to help guide decisions regarding patient treatment, which may include decisions to refer patients to specialists, to perform additional testing, or to assist in the selection of therapy. A distinctive feature of our approach is to combine multiple markers into a single, reportable index score that has higher diagnostic accuracy than its constituents. We concentrate on our development of novel diagnostic tests in the fields of gynecologic oncology and women's health, with an initial focus on ovarian cancer. We also intend to address clinical questions related to early disease detection, treatment response, monitoring of disease progression, prognosis and others through collaborations with leading academic and research institutions.

Our lead product, the OVA1® ovarian tumor triage test ("OVA1"), is a blood test designed to identify women who are at a high risk of having a malignant ovarian tumor prior to surgery. The United States Food and Drug Administration (the "FDA") cleared OVA1 in September 2009, and we commercially launched OVA1 in March 2010.

On June 23, 2014, Vermillion launched ASPiRA LABS, which specializes in applying biomarker-based technologies, including OVA1, to address critical needs in the management of gynecologic cancers. ASPiRA LABS provides expert diagnostic processing and results using a state-of-the-art biomarker-based diagnostic algorithm to inform clinical decision making and advance personalized treatment plans. In addition, ASPiRA LABS, a national lab based near Austin, Texas, seeks to serve as an educational and resource hub for healthcare professionals and women facing surgery for ovarian masses that are potentially cancerous and related gynecologic conditions. The lab processes diagnostic tests and clinical decision aids for women's health in ovarian cancer and plans to expand to other gynecologic conditions with high unmet need. ASPiRA began accepting samples on June 23, 2014. ASPiRA currently holds a Certificate of Registration under the Clinical Laboratory Improvement Amendments of 1988 ("CLIA") and a state laboratory license in California. ASPiRA is in the process of obtaining state licensure in New York, Florida, Rhode Island, Maryland and Pennsylvania.

We are focused on the execution of four core strategic business drivers in ovarian cancer diagnostics to build long-term value for our investors:

Maximizing the existing OVA1 opportunity in the United States by expanding our direct market reach, and payer coverage and commercialization of OVA1. This strategy includes the launch of a CLIA certified clinical laboratory, ASPiRA LABS in June 2014;

Improving OVA1 performance by seeking FDA clearance of a potentially better performing bio-marker panel while migrating OVA1 to a global testing platform;

Building an expanded patient base by seeking FDA approval and launching a next generation multi-marker ovarian cancer test to monitor patients at risk for ovarian cancer; and

Expanding our product offerings by adding additional gynecological tests such as longitudinal CA 125II testing. We believe that these business drivers will contribute significantly to addressing unmet medical needs for women faced with ovarian cancer and the continued development of our business.

Our Product

OVA1 addresses a clear clinical need, namely the pre-surgical identification of women who are at high risk of having a malignant ovarian tumor. Numerous studies have documented the benefit of referral of these women to gynecologic oncologists for their initial surgery. Prior to the clearance of OVA1, no blood test had been cleared by the FDA for physicians to use in the pre-surgical management of ovarian adnexal masses. OVA1 is a qualitative serum test that utilizes five well-established biomarkers and proprietary FDA-cleared software to determine the likelihood of malignancy in women over age 18, with a pelvic mass for whom surgery is planned. OVA1 was developed through large pre-clinical studies in collaboration with numerous academic medical centers encompassing over 2,500 clinical samples. OVA1 was fully validated in a prospective multi-center clinical trial encompassing 27 sites reflective of the diverse nature of the clinical centers at which ovarian adnexal masses are evaluated.

In 2012, we completed a second pivotal clinical study of OVA1 called the "OVA500 study," led by Dr. Robert E. Bristow, Director of Gynecologic Oncology Services with University of California Irvine Healthcare. The study evaluated OVA1 diagnostic performance in a population of 494 evaluable patients who underwent surgery for an adnexal mass after enrollment by a non-gynecologic oncologist. In February 2013, the OVA500 study was published in the peer-reviewed journal Gynecologic Oncology, which we believe enjoys the highest impact factor rating of any journal worldwide focused on gynecologic oncology. Since many professional medical societies stress the importance of multiple independent clinical trials as so-called "evidence levels", we also believe that the OVA500 study contributes to a higher evidence level relative to OVA1's utility in the medical management of adnexal masses.

In addition to these pivotal studies, three follow-on studies have been published bringing the number of full research articles on OVA1 clinical performance to a total of five peer-reviewed publications. Together, we believe these data provide strong clinical evidence that OVA1 improves the pre-surgical detection of ovarian cancer, across all stages or subtypes, in patients undergoing surgery for a suspicious ovarian mass.

The American Medical Association Current Procedural Terminology ("CPT®") Panel approved a Category I CPT code (81503) for OVA1, which became effective in January 2013.

Dr. Bristow presented another study at the Society of Gynecological Oncology ("SGO") in March 2013 which was published in the journal Obstetrics & Gynecology (also known as the Green Journal) in June 2013. This study was based on the medical records of 13,321 women with epithelial cancer, the most common type of ovarian cancer, diagnosed from 1999 to 2006 in California. Only 37 percent of these patients received treatment that adhered to guidelines set by the National Comprehensive Cancer Network ("NCCN"), an alliance of 23 major cancer centers with expert panels that analyze, research and recommend cancer treatments. The study found that surgeons who operated on 10 or more women a year for ovarian cancer, and hospitals that treated 20 or more a year, were more likely to adhere to NCCN guidelines and their patients lived longer. Among women with advanced disease — the stage at which ovarian cancer is usually first found — 35 percent survived at least five years if their care met the guidelines, compared with 26 percent of those whose care fell short.

In May 2013, SGO issued a new position statement on OVA1. This second SGO statement on OVA1 since its FDA clearance in 2009 represents another significant step toward acceptance of OVA1 as the standard of care for pre-surgically evaluating the risk of ovarian cancer in women with adnexal masses. The statement, titled "Multiplex Serum Testing for Women with Pelvic Mass", reads:

"Blood levels of five proteins in women with a known ovarian mass have been reported to change when ovarian cancer is present. Tests measuring these proteins may be useful in identifying women who should be referred to a gynecologic oncologist. Recent data have suggested that such tests, along with physician clinical assessment, may improve detection rates of malignancies among women with pelvic masses planning surgery. [1],[2] Results from such

tests should not be interpreted independently, nor be used in place of a physician's clinical assessment. Physicians are strongly encouraged to reference the American Congress of Obstetricians and Gynecologists' 2011 Committee Opinion "The Role of the Obstetrician-Gynecologist in the Early Detection of Epithelial Ovarian Cancer" to determine an appropriate care plan for their patients. It is important to note that no such test has been evaluated for use as, nor cleared by, the FDA as a screening tool for ovarian cancer. SGO does not formally endorse or promote any specific products or brands."

[1] Bristow RE, Smith A, Zhang Z, Chan DW, Crutcher G, Fung ET, et al. Ovarian malignancy risk stratification of the adnexal mass using a multivariate index assay. Gynecol Oncol 2013;128: 252–259

[2] Ueland FR, Desimone CP, Seamon LG, Miller RA, Goodrich S, Podzielinski I, et al. Effectiveness of a multivariate index assay in the preoperative assessment of ovarian tumors. Obstet Gynecol 2011;117:1289-1297.

We believe the position statement does two things:

- Lists as references the publications of OVA1's two pivotal clinical studies, comprised of the original FDA validation study published in June 2011 and the OVA500 "intended use" study published in 2013. Together, this offers an extensive, peer-reviewed proof source for physicians and payers to assess OVA1's clinical performance and comparative medical benefits versus today's standard of care.

Places OVA1 use in the context of current American Congress of Obstetricians and Gynecologists ("ACOG") practice guidelines, where CA125 has been used off-label for many years to predict malignancy before surgery, although with inferior performance.

In June 2013 our collaborators from Johns Hopkins Biomarker Discovery and Translation Center presented data from "proof of concept" work to identify markers with high clinical specificity that may complement OVA1. These results were presented in a poster at the annual meeting of the American Society for Clinical Oncology by Dr. Zhen Zhang and co-workers. The study identified a set of 5 biomarkers (CA125, prealbumin, IGFBP2, IL6 and FSH) which optimally reduced false positives among a targeted set of OVA1-positive benign patients. This panel was subsequently tested in a 50/50 cross-validation strategy against a sampling of OVA500 patients (N=384), to evaluate specificity and other diagnostic parameters. At a fixed sensitivity of 90%, the median specificity of models using the new panel in testing was 80.6%. The mean and median absolute improvements over that of OVA1 were 18.6% and 20.3%, respectively. The new panel demonstrated the possibility to improve specificity over that of the existing OVA1 algorithm, while maintaining a high sensitivity in pre-surgical assessment of malignancy. The work will be submitted for publication in 2014.

We are in the process of identifying intended use(s) and establishing a regulatory or commercial pathway for a potential next-generation OVA product utilizing this or another new panel. Any actual product development will likely differ significantly depending on a number of technical and commercial factors.

A study published in July 2014 in The American Journal of Obstetrics & Gynecology, examined the relationship between two imaging methods, ultrasound and computed tomography, and the OVA1 test result in assessing the risk of ovarian cancer among patients planning surgery for an ovarian mass. Using data obtained from 1,100 ovarian mass surgery patients in two previous pivotal trials of OVA1's clinical performance, conducted in 2007 and 2012, the study found that adding OVA1 reduced the number of ovarian cancers missed with imaging alone by 84-90%. Specifically, ultrasound alone missed 23.1% of ovarian cancers that were presented, but when OVA1 was added in parallel, the number of ovarian cancers missed decreased to 2.2%. When CT was used alone, 20.2% of ovarian cancers were missed but this rate fell to 2.9% when OVA1 was added in parallel. Additionally, the study found that when ultrasound and OVA1 were combined in parallel, 95% of ovarian cancers in a subgroup of early-stage patients were detected.

Novitas Solutions (formerly Highmark Medicare Services), a Medicare contractor, covers and reimburses for OVA1. In December 2013, the Centers for Medicare and Medicaid Services ("CMS") made its final determination and authorized Medicare contractors to set prices for Multianalyte Assays with Algorithmic Analyses ("MAAA") test CPT codes when they determine it is payable. CMS also validated that an algorithm has unique value by specifying that the gap-fill process and not cross-walk should be used by contractors to price MAAA tests. We expect OVA1 to be priced using the gap-fill method. We will be engaged in that process in 2014 for pricing effective January 1, 2015. This decision also sets a precedent for recognizing the value of biomarker developed tests to clinical decision-making and healthcare efficiencies.

Independent BlueCross BlueShield plans representing approximately 8.0 million lives provide coverage for OVA1. In total, including Medicare and other private payers, approximately 55.5 million patients have access to and coverage for OVA1.

Under the terms of our Strategic Alliance Agreement with Quest Diagnostics Incorporated ("Quest Diagnostics"), which we terminated in August 2013, Quest Diagnostics was required to pay us a fixed payment of $50 per OVA1 test performed, as well as 33% of its "gross margin" from revenue from performing OVA1 tests domestically, as that term is defined in the Strategic Alliance Agreement. Prior to the termination of the agreement, Quest Diagnostics had the right to be the exclusive clinical reference laboratory marketplace provider of OVA1 tests in its exclusive territory, which included the US, Mexico, the United Kingdom and India. This right extended through September 11, 2014, and Quest Diagnostics had the right to extend its exclusivity period for an additional year on the same terms and conditions. In August 2013, we sent Quest Diagnostics a notice of termination. Notwithstanding the termination, we agreed that Quest Diagnostics could continue to make OVA1 available to healthcare providers on the same financial terms following the termination while negotiating in good faith towards an alternative business structure. Quest Diagnostics has disputed the effectiveness of our notice of termination.

Corporate Information

We were originally incorporated in 1993, and we had our initial public offering in September 2000. Our executive offices are located at 12117 Bee Caves Road, Building Three, Suite 100, Austin, TX 78759, and our telephone number is (512) 519-0400. We maintain a website at www.vermillion.com and www.aspiralab.com where general information about us is available. Our websites, and the information contained therein, are not a part of this prospectus.

RISK FACTORS

Investing in our securities involves a high degree of risk. Please carefully consider the risk factors described in our most recent Annual Report on Form 10-K, any subsequent updates in our Quarterly Reports on Form 10-Q and any other filings we make with the SEC pursuant to Section 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), incorporated by reference herein, before making an investment decision. Additional risk factors may be included in any prospectus supplements relating to securities described in this prospectus. The occurrence of any of those risks could materially and adversely affect our business, prospects, financial condition, results of operations or cash flow. Other risks and uncertainties that we do not now consider to be material or of which we are not now aware may become important factors that affect us in the future and could result in a complete loss of your investment.

DISCLOSURE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus, any prospectus supplement and the documents that we incorporate herein or therein by reference contain forward-looking statements, as defined in the Private Securities Litigation Reform Act of 1995. These statements involve a number of risks and uncertainties that are difficult to predict. In some cases, you can identify forward-looking statements by words such as “may,” “expects,” “intends,” “anticipates,” “believes,” “estimates,” “plans,” “see “could,” “should,” “continue,” “will,” “potential,” “projects” or other similar expressions. Readers are cautioned that these forward-looking statements speak only as of the date on which the document in which they appear is filed with the SEC, and we do not assume any obligation to update, amend or clarify them to reflect events, new information or circumstances after such dates. Forward-looking statements are subject to risks, uncertainties and assumptions that are difficult to predict.

Examples of forward-looking statements regarding our business include the following:

- projections of or expectations regarding our future revenue, results of operations and financial condition;
- intentions to address clinical questions related to early disease detection, treatment response, monitoring of disease progression, prognosis and other issues in the fields of oncology and women’s health;
- anticipated efficacy of our products, product development activities and product innovations;
- our expected ability to consolidate the five OVA1 immunoassays on a single mainstream integrated diagnostic automation platform;
- expected competition and consolidation in the markets in which we compete;
- plans with respect to ASPiRA LABS;
- expectations regarding existing and future collaborations and partnerships;
- our belief that particular biomarker discoveries may have diagnostic and/or therapeutic utility;
- achieving milestones in product development, future regulatory or scientific submissions and presentations;
- our continued ability to comply with applicable governmental regulations;
- our continued ability to expand and protect our intellectual property portfolio;
- anticipated future losses;
- expected levels of expenditures;
- expected market adoption of our diagnostic tests, including OVA1;
- anticipated results of clinical trials, post-market studies required by FDA, and publications on OVA1;
- the amount of financing anticipated to be required to fund our planned operations;
- our prospects for obtaining support of medical or professional societies (e.g., SGO, NCCN and ACOG) through “guidelines”, “position statements” and the like;
- the financial or market share projections which could result from positive guidelines or position statements; and
- our expected reimbursement for our products, and our expected ability to obtain such reimbursement, from third-party payers such as private insurance companies and government insurance plans.

These statements involve estimates, assumptions and uncertainties that could cause actual results to differ materially from those expressed in them. Any forward-looking statements are qualified in their entirety by reference to the risk factors described in any accompanying prospectus supplement or in any document incorporated by reference into this prospectus. These factors include, among others:

- our ability to increase the volume of OVA1 sales;
- the fact that all of our revenue was derived from Quest Diagnostics during 2013 and that there is no guarantee that we will be able to successfully market our test through additional channels in the future;
- the consequences of terminating the Quest Diagnostics Strategic Alliance Agreement;
- failures by third-party payers to reimburse OVA1 or changes or variances in reimbursement rates;
- our ability to secure adequate funds on terms acceptable to us;

- our ability to commercialize OVA1 outside the United States;
- our ability to develop additional diagnostic products and achieve significant commercial market acceptance of such products;
- competition in the diagnostics market;
- delay by or failure of the FDA to approve our diagnostic tests submitted to the FDA;
- failure to comply with FDA requirements for production, marketing and postmarket monitoring of our products;
- the continuity of supply of our biomarker kits;
- our ability to continue to develop our technologies;
- our ability to use, maintain and protect our intellectual property rights;
- our ability to recruit and retain key executives and employees;
- changes in law or healthcare policy;
- low liquidity and trading volume of our common stock may be low and the concentration of our stock ownership; and
- volatility of our stock price.

You should read this prospectus, any accompanying prospectus supplement, any related free writing prospectus and the documents that we reference herein and therein and have filed as exhibits to the registration statement, of which this prospectus is part, completely and with the understanding that our actual future results may be materially different from what we currently expect. You should not put undue reliance on any forward-looking statement. We believe it is important to communicate our expectations to our investors. However, there may be events in the future that we are not able to accurately predict or that we do not fully control that could cause actual results to differ materially from those expressed or implied in our forward-looking statements.

USE OF PROCEEDS

Unless otherwise indicated in the prospectus supplement, we will use the net proceeds from the sale of securities offered by this prospectus for general corporate purposes, including working capital, for further research and development and ongoing sales and marketing expenses, and, potentially, capital expenditures and licensing of additional technologies. We may also use a portion of the net proceeds from this offering to acquire or invest in complimentary businesses, technologies, product candidates or other intellectual property, although we have no present commitments or agreements to do so. The timing and amount of our actual expenditures will be based on many factors, including cash flows from operations and the anticipated growth of our business. As a result, unless otherwise indicated in the prospectus supplement, our management will have broad discretion to allocate the net proceeds of the offerings. Pending their ultimate use, we intend to invest the net proceeds in short-term, investment-grade, interest-bearing instruments.

PLAN OF DISTRIBUTION

We may sell the securities offered through this prospectus in one or more of the following ways (or in any combination) from time to time:

- to or through underwriters or dealers;
- directly to purchasers, including our affiliates;
- through agents; or
- a combination of any these methods.

If underwriters or dealers are used in the sale, the securities will be acquired by the underwriters or dealers for their own account and may be resold from time to time in one or more transactions, including:

- in one or more transactions at a fixed price or prices, which may be changed from time to time;
- in “at-the-market offerings,” within the meaning of Rule 415(a)(4) of the Securities Act, to or through a market maker or into an existing trading market, on an exchange or otherwise;
- through a market maker or into an existing trading market on an exchange or otherwise;
- at prices related to those prevailing market prices; or
- at negotiated prices.

The prospectus supplement will include the following information:

- the terms of the offering;
- the names of any underwriters or agents;
- the name or names of any managing underwriter or underwriters;
- the purchase price of the securities;
- the net proceeds from the sale of the securities;
- any delayed delivery arrangements;
- any underwriting discounts, commissions and other items constituting underwriters' compensation;
- any initial public offering price;
- any discounts or concessions allowed or reallowed or paid to dealers; and
- any commissions paid to agents.

Sale Through Underwriters or Dealers

If underwriters are used in the sale of any securities, the underwriters will acquire the securities for their own account, including through underwriting, purchase, security lending or repurchase agreements with us. The underwriters may resell the securities from time to time in one or more transactions, including negotiated transactions. Underwriters may sell the securities in order to facilitate transactions in any of our other securities (described in this prospectus or otherwise), including other public or private transactions and short sales. Underwriters may offer securities to the public either through underwriting syndicates represented by one or more managing underwriters or directly by one or more firms acting as underwriters. Unless otherwise indicated in the prospectus supplement, the obligations of the underwriters to purchase the securities will be subject to certain conditions, and the underwriters

will be obligated to purchase all the offered securities if they purchase any of them. The underwriters may change from time to time any initial public offering price and any discounts or concessions allowed or reallowed or paid to dealers. The prospectus supplement will include the names of the principal underwriters, the respective amount of securities underwritten, the nature of the obligation of the underwriters to take the securities and the nature of any material relationship between an underwriter and us.

If dealers are used in the sale of securities offered through this prospectus, we will sell the securities to them as principals. They may then resell those securities to the public at varying prices determined by the dealers at the time of resale. The prospectus supplement will include the names of the dealers and the terms of the transaction.

We may authorize underwriters, dealers or agents to solicit offers by certain purchasers to purchase our securities from us at the public offering price set forth in the prospectus supplement pursuant to delayed delivery contracts providing for payment and delivery on a specified date in the future. The contracts will be subject to those conditions set forth in the prospectus supplement, and the prospectus supplement will set forth any commissions paid for solicitation of these contracts.

Underwriters, dealers and agents may contract for or otherwise be entitled to indemnification by us against certain civil liabilities, including liabilities under the Securities Act, or to contribution with respect to payments made by the underwriters, dealers or agents, under agreements between us on one hand, and the underwriters, dealers and agents, on the other hand.

We may grant underwriters who participate in the distribution of our securities an option to purchase additional securities to cover over-allotments, if any, in connection with the distribution.

Underwriters, dealers, or agents may receive compensation in the form of discounts, concessions or commissions from us or our purchasers, as their agents in connection with the sale of our securities. These underwriters, dealers or agents may be considered to be underwriters under the Securities Act. As a result, discounts, commissions or profits on resale received by the underwriters, dealers or agents may be treated as underwriting discounts and commissions. The prospectus supplement for any securities offered by us will identify any such underwriter, dealer or agent and describe any compensation received by them from us or the selling stockholders. Any public offering price and any discounts or concessions allowed or re-allowed or paid to dealers may be changed from time to time.

Underwriters, broker-dealers or agents who may become involved in the sale of our securities may engage in transactions with and perform other services for us for which they receive compensation.

Direct Sales and Sales Through Agents

We may sell the securities offered through this prospectus directly. In this case, no underwriters or agents would be involved. Such securities may also be sold through agents designated from time to time. The prospectus supplement will name any agent involved in the offer or sale of the offered securities and will describe any commissions payable to the agent by us. Unless otherwise indicated in the prospectus supplement, any agent will agree to use its reasonable best efforts to solicit purchases for the period of its appointment.

We may sell the securities directly to institutional investors or others who may be deemed to be underwriters within the meaning of the Securities Act, with respect to any sale of those securities.

At-the-Market Offerings

To the extent that we make sales through one or more underwriters or agents in at-the-market offerings, we will do so pursuant to the terms of a sales agency financing agreement or other at-the-market offering arrangement between us, on one hand, and the underwriters or agents, on the other. If we engage in at-the-market sales pursuant to any such

agreement, we will issue and sell our securities through one or more underwriters or agents, which may act on an agency basis or a principal basis. During the term of any such agreement, we may sell securities on a daily basis in exchange transactions or otherwise as we agree with the underwriters or agents. Any such agreement will provide that any securities sold will be sold at prices related to the then prevailing market prices for our securities. Therefore, exact figures regarding proceeds that will be raised or commissions to be paid cannot be determined at this time. Pursuant to the terms of the agreement, we may agree to sell, and the relevant underwriters or agents may agree to solicit offers to purchase blocks of our common stock or other securities. The terms of any such agreement will be set forth in more detail in the prospectus supplement.

Market Making, Stabilization and Other Transactions

In connection with an offering through underwriters, an underwriter may, to the extent permitted by applicable rules and regulations, purchase and sell securities in the open market. These transactions, to the extent permitted by applicable rules and regulations, may include short sales, stabilizing transactions and purchases to cover positions created by short sales. Short sales involve the sale by the underwriters of a greater number of securities than they are required to purchase in the offering. “Covered” short sales are short sales made in an amount not greater than the underwriters’ option to purchase additional securities from us in the

offering, if any. If the underwriters have an over-allotment option to purchase additional securities from us, the underwriters may consider, among other things, the price of securities available for purchase in the open market as compared to the price at which they may purchase securities through the over-allotment option. “Naked” short sales, which may be prohibited or restricted by applicable rules and regulations, are any sales in excess of such option or where the underwriters do not have an over-allotment option. The underwriters must close out any naked short position by purchasing securities in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the securities in the open market after pricing that could adversely affect investors who purchase in the offering.

Accordingly, to cover these short positions or to otherwise stabilize or maintain the price of the securities, the underwriters may bid for or purchase securities in the open market and may impose penalty bids. If penalty bids are imposed, selling concessions allowed to syndicate members or other broker-dealers participating in the offering are reclaimed if securities previously distributed in the offering are repurchased, whether in connection with stabilization transactions or otherwise. The effect of these transactions may be to stabilize or maintain the market price of the securities at a level above that which might otherwise prevail in the open market. The imposition of a penalty bid may also affect the price of the securities to the extent that it discourages resale of the securities. The magnitude or effect of any stabilization or other transactions is uncertain.

Derivative Transactions and Hedging

We, the underwriters or other agents may engage in derivative transactions involving the securities. These derivatives may consist of short sale transactions and other hedging activities. The underwriters or agents may acquire a long or short position in the securities, hold or resell securities acquired and purchase options or futures on the securities and other derivative instruments with returns linked to or related to changes in the price of the securities. In order to facilitate these derivative transactions, we may enter into security lending or repurchase agreements with the underwriters or agents. The underwriters or agents may effect the derivative transactions through sales of the securities to the public, including short sales, or by lending the securities in order to facilitate short sale transactions by others. The underwriters or agents may also use the securities purchased or borrowed from us or others (or, in the case of derivatives, securities received from us in settlement of those derivatives) to directly or indirectly settle sales of the securities or close out any related open borrowings of the securities.

Trading Market and Listing of Securities

Any common stock sold or resold pursuant to a prospectus supplement will be listed on The NASDAQ Capital Market or on such other national securities exchange as our common stock may then be listed. The securities other than common stock may or may not be listed on a national securities exchange. It is possible that one or more underwriters may make a market in a class or series of securities, but the underwriters will not be obligated to do so and may discontinue any market making at any time without notice. We cannot give any assurance as to the liquidity of the trading market for any of the securities.

General Information

Agents, underwriters, and dealers may be entitled, under agreements entered into with us, to indemnification by us against certain liabilities, including liabilities under the Securities Act.

DESCRIPTION OF CAPITAL STOCK

The following summary description of our capital stock is based on the applicable provisions of the Delaware General Corporation Law, or DGCL, and on the provisions of our Fourth Amended and Restated Certificate of Incorporation, dated January 22, 2010, as amended effective June 19, 2014 (our "Certificate of Incorporation"), and our Fifth Amended and Restated Bylaws, effective June 19, 2014 (our "Bylaws"). This information is qualified entirely by reference to the applicable provisions of the DGCL, our Certificate of Incorporation, and our Bylaws. For information on how to obtain copies of our Certificate of Incorporation and our Bylaws, please refer to the heading "Where You Can Find More Information" in this prospectus.

Our Authorized Capital Stock

Under our Certificate of Incorporation, our authorized capital stock consists of 150,000,000 shares of common stock, par value $0.001 per share, and 5,000,000 shares of preferred stock, par value $0.001 per share.

Common Stock

As of August 31, 2014, we had 35,897,776 shares of our common stock outstanding, 1,796,692 shares of our common stock that were subject to outstanding options, 47,500 shares of our common stock subject to existing restricted stock grants and 952,881 shares of our common stock reserved for future issuance to employees, directors and consultants pursuant to our stock incentive plans. In addition, as of August 31, 2014, warrants to purchase 483,359 shares of our common stock were outstanding at exercise prices ranging from $1.46 to $4.70 per share, with a weighted average exercise price of $1.65 per share. All outstanding shares of common stock are, and the shares of common stock offered by us in this offering, when issued and paid for will be, fully paid and nonassessable. The rights, preferences and privileges of the holders of common stock are subject to, and may be adversely affected by, the rights of the holders of shares of any series of preferred stock which we may designate in the future.

Voting Rights

Each holder of common stock is entitled to one vote for each share on all matters to be voted upon by the stockholders, and there are no cumulative voting rights.

Dividend Rights

Subject to preferences to which holders of preferred stock may be entitled and the rights of certain of our stockholders set forth in the Stockholders Agreement (as defined below), holders of common stock are entitled to receive ratably such dividends, if any, as may be declared from time to time by our Board of Directors out of funds legally available therefor. We have never paid or declared any dividend on our common stock, and we do not anticipate paying cash dividends on any common stock in the foreseeable future. We intend to retain all available funds and any future earnings to fund the development and expansion of our business.

No Preemptive or Similar Rights

Holders of our common stock do not have preemptive rights, and our common stock is not convertible or redeemable. As described under "Stockholders Agreement," certain holders of our common stock have the right to purchase shares in connection with most equity offerings made by the Company.

Right to Receive Liquidation Distributions

In the event of our liquidation, dissolution or winding up, holders of common stock would be entitled to share in our assets remaining after the payment of liabilities and the satisfaction of any liquidation preference granted the holders of any outstanding shares of any senior class of securities. The rights, preferences and privileges of the holders of common stock are subject to, and may be adversely affected by, the rights of the holders of shares of any series of preferred stock which we may designate in the future.

Preferred Stock

There are no shares of our preferred stock outstanding.

Our Board of Directors is authorized, subject to any limitations prescribed by law, without stockholder approval, to issue from time to time up to an aggregate of 5,000,000 shares of preferred stock, in one or more series, each of such series to have such rights and preferences, including voting rights, dividend rights, conversion rights, redemption terms and liquidation preferences as shall be determined by our Board of Directors. Any issuance of shares of preferred stock could adversely affect the voting power of holders of

common stock, and the likelihood that the holders of preferred stock will receive dividend payments and payments upon liquidation could have the effect of delaying, deferring or preventing a change in control.

Warrants

As of August 31, 2014, warrants to purchase 483,359 shares of common stock at exercise prices ranging from $1.46 to $4.70 were outstanding, with a weighted exercise price of $1.65 per share. All outstanding warrants contain provisions for the adjustment of the exercise price in the event of stock dividends, stock splits, reorganizations, reclassifications or mergers. In addition, 70,000 of the warrants contain a “cashless exercise” feature that allows the holders thereof to exercise the warrants without a cash payment to us under certain circumstances. Liolios Group, Inc., which holds warrants to purchase 70,000 shares of our common stock, has the right to exercise “piggyback” registration rights for any registration statements that we file on our own account or the account of others with respect to shares of our common stock. These “piggyback” registration rights expire with respect to 21,000 of the shares underlying such warrants on each of October 31, 2014, April 30, 2015, October 31, 2015 and with respect to 7,000 of the shares underlying such warrants on April 30, 2016. The rights of the shares of common stock issuable upon exercise of all of our outstanding warrants are the same as those described under “Common Stock” above.

We may issue warrants to purchase shares of common stock or shares of preferred stock, independently or together with other securities. Warrants sold with other securities may be attached to or separate from the other securities. We will issue warrants under one or more warrant agreements between us and a warrant agent we will name in the prospectus supplement.

The prospectus supplement relating to any warrants we are offering will include specific terms relating to the offering. These terms will include some or all of the following:

- the aggregate number of warrants offered;
- the title of the warrants;
- the designation, number and terms of the shares of common stock or shares of preferred stock purchasable upon exercise of the warrants and procedures by which those numbers may be adjusted;
- the exercise price of the warrants;
- the dates or periods during which the warrants are exercisable;

- the designation and terms of any securities with which the warrants are issued;

- if the warrants are issued as a unit with another security, the date on and after which the warrants and the other security will be separately transferable;

- if the exercise price is not payable in U.S. dollars, the foreign currency, currency unit or composite currency in which the exercise price is denominated;

- any minimum or maximum amount of warrants that may be exercised at any one time;

- any terms relating to the modification of the warrants; and.
- any terms, procedures and limitations relating to the transferability, exchange or exercise of the warrants.

Rights

We may issue rights for the purchase of shares of our common stock or shares of our preferred stock. Each series of rights will be issued under a separate rights agreement which we will enter into with a bank or trust company, as rights agent, all as set forth in the applicable prospectus supplement. The rights agent will act solely as our agent in connection with the certificates relating to the rights and will not assume any obligation or relationship of agency or trust with any holders of rights certificates or beneficial owners of rights. We will file the rights agreement and the rights certificates relating to each series of rights with the SEC and incorporate them by reference as an exhibit to the registration statement of which this prospectus is a part on or before the time we issue a series of rights.

The applicable prospectus supplement will describe the terms of any rights we issue, including as applicable:

- the date for determining the persons entitled to participate in the rights distribution;

- the aggregate number or amount of underlying securities purchasable upon exercise of the rights and the exercise price;

- the aggregate number of rights being issued;

- the date, if any, on and after which the rights may be transferable separately;

- the date on which the right to exercise the rights commences and the date on which such right expires;
- the designation and terms of any securities with which the warrants are issued;
- a discussion of any material or special U.S. federal income tax considerations applicable to the rights; and
- any other terms of the rights, including the terms, procedures and limitations relating to the distribution, exchange and exercise of the rights.

Rights will be exercisable for U.S. dollars only and will be in registered form only.

Units

We may issue securities in units, each consisting of two or more types of securities. For example, we might issue units consisting of a combination of common stock and warrants to purchase common stock. If we issue units, the prospectus supplement relating to the units will contain the information described above with regard to each of the securities that is a component of the units. In addition, the prospectus supplement relating to the units will describe the terms of any units we issue, including as applicable:

- the date, if any, on and after which the units may be transferable separately;
- whether we will apply to have the units traded on a securities exchange or securities quotation system;
- a discussion of any material or special U.S. federal income tax considerations applicable to the units; and
- how, for U.S. federal income tax purposes, the purchase price paid for the units is to be allocated among the component securities.

Stockholders Agreement

In connection with a private placement in May 2013, we entered into a stockholders agreement with the purchasers named in that agreement. Pursuant to and subject to the terms of the stockholders agreement, certain of the investors received rights to participate in any future equity offerings on the same price and terms as other investors, and rights to exercise “piggyback” registration rights for any registration statements that we file prior to May 13, 2018 on our own account or for the account of others with respect to shares of our common stock. Some or all of such investors might participate in one or more of the equity offerings under the registration statement of which this prospectus is a part.

In addition, the stockholders agreement prohibits the company from taking material actions without the consent of at least one of the two primary investors. These material actions include:

- making any acquisition with value greater than $2 million;

• entering into, or amending the terms of agreements with Quest Diagnostics Incorporated, provided that such investors' consent shall not be unreasonably withheld, conditioned or delayed following good faith consultation with the company;

• submitting any resolution at a meeting of stockholders or in any other manner changing or authorizing a change in the size of our Board of Directors;

• offering, selling or issuing any securities senior to our common stock or any securities that are convertible into or exchangeable or exercisable for securities ranking senior to our common stock;

• amending our Certificate of Incorporation or our Bylaws in any manner that affects the rights, privileges or economics of our common stock or the warrants purchased in the May 2013 private placement;

• taking any action that would result in a change in control of Vermillion or an insolvency event;

• paying or declaring dividends on any securities of the company or distributing any assets of the company other than in the ordinary course of business or repurchasing any outstanding securities of the company; or

• adopting or amending any shareholder rights plan.

In addition, the two primary investors each received the right to designate a person to serve on our Board of Directors. These rights terminate for each stockholder when that stockholder ceases to beneficially own less than 50% of the shares and warrants (taking into account shares issued upon exercise of the warrants), in the aggregate, than were purchased at the closing of the private placement.

Section 203 of the Delaware Corporation Law

We are subject to Section 203 of the DGCL, which prevents an "interested stockholder" (defined in Section 203 of the DGCL, generally, as a person owning 15% or more of a corporation's outstanding voting stock), from engaging in a "business combination" (as defined in Section 203 of the DGCL) with a publicly-held Delaware corporation for three years following the date such person became an interested stockholder, unless:

- before such person became an interested stockholder, the board of directors of the corporation approved the transaction in which the interested stockholder became an interested stockholder or approved the business combination;
- upon consummation of the transaction that resulted in the interested stockholder's becoming an interested stockholder, the interested stockholder owns at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced (excluding stock held by directors who are also officers of the corporation and by employee stock plans that do not provide employees with the rights to determine confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer); or
- following the transaction in which such person became an interested stockholder, the business combination is approved by the board of directors of the corporation and authorized at a meeting of stockholders by the affirmative vote of the holders of two-thirds of the outstanding voting stock of the corporation not owned by the interested stockholder.

The provisions of Section 203 of the DGCL could make a takeover of our company difficult.

Effect of Certain Provisions of Our Certificate of Incorporation and Bylaws

Certain provisions of our Certificate of Incorporation and Bylaws may have the effect of making it more difficult for a third party to acquire, or of discouraging a third party from attempting to acquire, control of us. Such provisions could limit the price that certain investors might be willing to pay in the future for our securities. Our Certificate of Incorporation eliminates the right of stockholders to call special meetings of stockholders or to act by written consent without a meeting, and our Bylaws require advance notice for stockholder proposals and director nominations, which may preclude stockholders from bringing matters before an annual meeting of stockholders or from making nominations for directors at an annual meeting of stockholders. Our Certificate of Incorporation authorizes undesignated preferred stock, which makes it possible for our Board of Directors to issue preferred stock with voting or other rights or preferences that could impede the success of any attempt to change control of us.

These and other provisions may have the effect of deferring hostile takeovers or delaying changes in control or management of us. The amendment of any of the provisions of our Certificate of Incorporation described in the immediately preceding paragraph would require approval by our Board of Directors and the affirmative vote of at least 66 2/3% of our then outstanding voting securities, and the amendment of any of the provisions of our Bylaws described in the immediately preceding paragraph would require approval by our Board of Directors or the affirmative vote of at least 66 2/3% of our then outstanding voting securities.

Transfer Agent

The transfer agent for our common stock is Wells Fargo Shareowner Services.

Listing

Our common stock is listed on The NASDAQ Capital Market under the symbol "VRML."

LEGAL MATTERS

Sidley Austin LLP will pass upon the validity of the securities being registered by the registration statement of which this prospectus is a part. Additional legal matters may be passed upon for us or any underwriters, dealers or agents, by counsel that we will name in the applicable prospectus supplement.

EXPERTS

The consolidated financial statements as of December 31, 2013 and 2012 and for the years then ended incorporated by reference in this prospectus have been so incorporated in reliance on the report of BDO USA, LLP, an independent registered public accounting firm, incorporated herein by reference, given on the authority of said firm as experts in auditing and accounting.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and current reports, proxy statements and other information with the SEC. We have filed with the SEC a registration statement on Form S-3 under the Securities Act with respect to the securities we are offering under this prospectus. This prospectus does not contain all of the information set forth in the registration statement and the exhibits to the registration statement. For further information with respect to us and the securities we are offering under this prospectus, we refer you to the registration statement and the exhibits and schedules filed as a part of the registration statement. You may read and copy the registration statement, as well as our reports, proxy statements and other information, at the SEC's Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for more information about the operation of the Public Reference Room. The SEC maintains an Internet site that contains reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC, including Vermillion, Inc. The SEC's Internet site can be found at http://www.sec.gov.

Information on any Vermillion website, any subsection, page, or other subdivision of any Vermillion website, or any website linked to by content on any Vermillion website, is not part of this prospectus and you should not rely on that information unless that information is also in this prospectus or incorporated by reference in this prospectus.

IMPORTANT INFORMATION INCORPORATED BY REFERENCE

The SEC allows us to "incorporate by reference" information into this prospectus, which means that we can disclose important information to you by referring you to another document filed separately with the SEC. The documents incorporated by reference into this prospectus contain important information that you should read about us.

The following documents are incorporated by reference into this prospectus:

(a) The registrant's Annual Report on Form 10-K for the fiscal year ended December 31, 2013 filed with the SEC on March 31, 2014;
(b) The registrant's Quarterly Report on Form 10-Q for the quarters ended March 31, 2014 and June 30, 2014 filed with the SEC on May 15, 2014 and August 14, 2014, respectively;
(c) The registrant's Current Reports on Form 8-K filed with the SEC on (i) January 3, 2014, (ii) March 10, 2014, (iii) March 31, 2014, (iv) April 15, 2014, (v) April 18, 2014, (vi) April 23, 2014, (vii) June 24, 2014, (vii) July 28, 2014, (ix) August 15, 2014 and (x) August 21, 2014;
(d) The description of the registrant's common stock set forth in the Registration Statement on Form S-1 filed with the SEC on February 21, 2011 (File No. 333-171797), including any amendments or reports filed for the purpose of updating such description.

We also incorporate by reference any future filings (other than current reports furnished under Item 2.02 or Item 7.01 of Form 8-K and exhibits filed on such form that are related to such items unless such Form 8-K expressly provides to the contrary) made with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act, including those made after the date of the initial filing of the registration statement of which this prospectus is a part and prior to effectiveness of such registration statement, until we file a post-effective amendment that indicates the termination of the offering of the securities made by this prospectus and will become a part of this prospectus from the respective dates that such documents are filed with the SEC. Any statement contained herein or in a document incorporated or deemed to be incorporated by reference herein shall be deemed to be modified or superseded for purposes hereof or of the related prospectus supplement to the extent that a statement contained herein or in any other subsequently filed document which is also incorporated or deemed to be incorporated herein modifies or supersedes such statement. Any such statement so modified or superseded shall not be deemed, except as so modified or superseded, to constitute a

part of this prospectus.

Documents incorporated by reference are available from us, without charge. You may obtain documents incorporated by reference in this prospectus by requesting them in writing or by telephone at the following address:

Vermillion, Inc.

12117 Bee Caves Road, Building Three, Suite 100

Austin, Texas 78738

(512) 519-0400
Attn: Corporate Secretary

Vermillion, Inc.

PROSPECTUS

$50,000,000

Common Stock, Preferred Stock,
Warrants, Rights and Units

, 2014

The information in this prospectus is not complete and may be changed. We may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities, and we are not soliciting offers to buy these securities, in any state or other jurisdiction where the offer or sale is not permitted.

SUBJECT TO COMPLETION, DATED SEPTEMBER 12, 2014

PROSPECTUS

Up to $15,000,000 of Shares

Common Stock

We have entered into a Controlled Equity Offering sales agreement with Cantor Fitzgerald & Co. relating to shares of our common stock offered by this at-the-market offering prospectus and the accompanying base prospectus. In accordance with the terms of the sales agreement, we may offer and sell shares of our common stock having an aggregate offering price of up to $15,000,000 from time to time through Cantor Fitzgerald & Co., acting as agent.

Our common stock is listed on The NASDAQ Capital Market under the symbol “VRML.” On September 11, 2014, the last reported sale price of our common stock on The NASDAQ Capital Market was $2.21 per share. As of September 12, 2014, the aggregate market value of our outstanding common stock held by our non-affiliates, as calculated pursuant to the rules of the Securities and Exchange Commission, was $47,592,445. Pursuant to General Instruction I.B.6 of Form S-3, in no event will we sell securities in a public primary offering with a value exceeding more than one-third of our “public float” (the market value of our common stock held by our non-affiliates) in any 12-month period so long as our public float remains below $75,000,000. We have not sold any of our common stock or securities convertible into our common stock during the 12 calendar months prior to and including the date of this prospectus.

Sales of our common stock, if any, under this at-the-market offering prospectus and the accompanying base prospectus may be made in sales deemed to be “at-the-market” equity offerings as defined in Rule 415 promulgated under the Securities Act of 1933, as amended, or the Securities Act, including sales made directly on or through The NASDAQ Capital Market, the existing trading market for our common stock, sales made to or through a market maker other than on an exchange or otherwise, in negotiated transactions at market prices prevailing at the time of sale or at prices related to such prevailing market prices, and/or any other method permitted by law. Cantor Fitzgerald & Co. will act as sales agent on a best effort basis and use commercially reasonable efforts to sell on our behalf all of the shares of common stock requested to be sold by us, consistent with its normal trading and sales practices, on mutually agreed terms between Cantor Fitzgerald & Co. and us. There is no arrangement for funds to be received in any escrow, trust or similar arrangement.

Except as otherwise described in the sales agreement, Cantor Fitzgerald & Co. will be entitled to compensation at a fixed commission rate of up to 3.0% of the gross sales price per share sold. In connection with the sale of the common stock on our behalf, Cantor Fitzgerald & Co. will be deemed to be an "underwriter" within the meaning of the Securities Act, and the compensation of Cantor Fitzgerald & Co. will be deemed to be underwriting commissions or discounts.

Investing in our securities involves a high degree of risk. Before making an investment decision, please read the information contained in or incorporated by reference under the heading "Risk Factors" beginning on page S-6 of this at-the-market offering prospectus, on page 5 of the accompanying base prospectus and in the documents incorporated by reference into this at-the-market offering prospectus.

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

The date of this prospectus is , 2014.

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ABOUT THIS AT-THE-MARKET OFFERING PROSPECTUS

This at-the-market offering prospectus is part of a registration statement that we have filed with the Securities and Exchange Commission, or SEC, utilizing a "shelf" registration process. Under the shelf registration process, we may offer shares of our common stock having an aggregate offering price of up to $15,000,000 from time to time under this at-the-market offering prospectus at prices and on terms to be determined by market conditions at the time of offering. This document is comprised of two parts. The first part is the accompanying base prospectus (including the documents incorporated by reference into the accompanying base prospectus), which provides more general information, some of which may not apply to this offering. The second part is this at-the-market offering prospectus, which describes the specific terms of this offering and also adds to, and updates information contained in, the accompanying base prospectus and the documents incorporated by reference into this at-the-market offering prospectus and the accompanying base prospectus. Generally, when we refer to this "prospectus," we are referring to the combined document consisting of this at-the-market offering prospectus and the accompanying base prospectus. If information in this at-the-market offering prospectus is inconsistent with the accompanying base prospectus or any document incorporated by reference into this at-the-market offering prospectus or the base prospectus that was filed before the date of this at-the-market-offering prospectus, you should rely on this prospectus. However, if any statement in one of these documents is inconsistent with a statement in another document having a later date—for example, a future filing incorporated by reference in this prospectus—the statement in the document having the later date modifies or supersedes the earlier statement as our business, financial condition, results of operations and prospects may have changed since the earlier dates.

You should rely only on the information contained in, or incorporated by reference into, this at-the-market offering prospectus, the accompanying base prospectus and any free writing prospectus that we have authorized for use in connection with this offering. We have not authorized any other person to provide you with different information. We are not making an offer to sell or soliciting an offer to buy our securities in any jurisdiction in which an offer or solicitation is not authorized or in which the person making that offer or solicitation is not qualified to do so or to anyone to whom it is unlawful to make an offer or solicitation. You should assume that the information appearing in this at-the-market offering prospectus, the accompanying base prospectus, the documents incorporated by reference into this at-the-market offering prospectus and the accompanying base prospectus and any free writing prospectus that we have authorized for use in connection with this offering is accurate only as of the date of those respective documents. Our business, financial condition, results of operations and prospects may have changed since those dates. You should read this at-the-market offering prospectus, the accompanying base prospectus, the documents incorporated by reference into this at-the-market offering prospectus and the accompanying base prospectus and any free writing prospectus that we have authorized for use in connection with this offering in their entirety before making an investment decision. You should also read and consider the information in the documents to which we have referred you in the sections of this at-the-market offering prospectus entitled "Where You Can Find More Information" and "Incorporation of Certain Information by Reference." The information incorporated by reference is considered part of this at-the-market offering prospectus, and information we file later with the SEC may automatically update and supersede this information.

Unless the context otherwise requires, as used in this at-the-market offering prospectus, "we," "us," "Vermillion, Inc.," "Vermillion," "the Company" and "our" refer to Vermillion, Inc., a Delaware corporation.

AT-THE-MARKET OFFERING PROSPECTUS SUMMARY

This summary highlights certain information contained in greater detail elsewhere in this at-the-market offering prospectus or incorporated by reference into this at-the-market offering prospectus. This summary is not complete and does not contain all of the information that you should consider before deciding whether to invest in our securities. You should carefully read this at-the-market offering prospectus , the accompanying base prospectus, any related free writing prospectus that we have authorized for use in connection with this offering and the documents incorporated by reference herein and in the accompanying base prospectus, including the information referred to under the heading "Risk Factors" in this at-the-market offering prospectus on page S-6, in the accompanying base prospectus on page 5 and in the documents incorporated by reference into this at-the-market offering prospectus.

Our Company

Our vision is to drive advancement in personalized medical management — initially focused on ovarian health — to improve outcomes for patients, physicians and providers.

We are dedicated to the discovery, development and commercialization of novel high-value diagnostic tests that help physicians diagnose, treat and improve outcomes for patients. Our tests are intended to help guide decisions regarding patient treatment, which may include decisions to refer patients to specialists, to perform additional testing, or to assist in the selection of therapy. A distinctive feature of our approach is to combine multiple markers into a single, reportable index score that has higher diagnostic accuracy than its constituents. We concentrate on our development of novel diagnostic tests in the fields of gynecologic oncology and women's health, with an initial focus on ovarian cancer. We also intend to address clinical questions related to early disease detection, treatment response, monitoring of disease progression, prognosis and others through collaborations with leading academic and research institutions.

Our lead product, the OVA1® ovarian tumor triage test ("OVA1"), is a blood test designed to identify women who are at a high risk of having a malignant ovarian tumor prior to surgery. The United States Food and Drug Administration (the "FDA") cleared OVA1 in September 2009, and we commercially launched OVA1 in March 2010.

On June 23, 2014, Vermillion launched ASPiRA LABS, which specializes in applying biomarker-based technologies, including OVA1, to address critical needs in the management of gynecologic cancers. ASPiRA LABS provides expert diagnostic processing and results using a state-of-the-art biomarker-based diagnostic algorithm to inform clinical decision making and advance personalized treatment plans. In addition, ASPiRA LABS, a national lab based near Austin, Texas, seeks to serve as an educational and resource hub for healthcare professionals and women facing surgery for ovarian masses that are potentially cancerous and related gynecologic conditions. The lab processes diagnostic tests and clinical decision aids for women's health in ovarian cancer and plans to expand to other gynecologic conditions with high unmet need. ASPiRA began accepting samples on June 23, 2014. ASPiRA currently holds a Certificate of Registration under the Clinical Laboratory Improvement Amendments of 1988 ("CLIA") and a state laboratory license in California. ASPiRA is in the process of obtaining state licensure in New York, Florida, Rhode Island, Maryland and Pennsylvania.

We are focused on the execution of four core strategic business drivers in ovarian cancer diagnostics to build long-term value for our investors:

Maximizing the existing OVA1 opportunity in the United States by expanding our direct market reach, and payer coverage and commercialization of OVA1. This strategy includes the launch of a CLIA certified clinical laboratory, ASPiRA LABS in June 2014;

Improving OVA1 performance by seeking FDA clearance of a potentially better performing bio-marker panel while migrating OVA1 to a global testing platform;

Building an expanded patient base by seeking FDA approval and launching a next generation multi-marker ovarian cancer test to monitor patients at risk for ovarian cancer; and

Expanding our product offerings by adding additional gynecological tests such as longitudinal CA 125II testing. We believe that these business drivers will contribute significantly to addressing unmet medical needs for women faced with ovarian cancer and the continued development of our business.

Our Product

OVA1 addresses a clear clinical need, namely the pre-surgical identification of women who are at high risk of having a malignant ovarian tumor. Numerous studies have documented the benefit of referral of these women to gynecologic oncologists for

their initial surgery. Prior to the clearance of OVA1, no blood test had been cleared by the FDA for physicians to use in the pre-surgical management of ovarian adnexal masses. OVA1 is a qualitative serum test that utilizes five well-established biomarkers and proprietary FDA-cleared software to determine the likelihood of malignancy in women over age 18, with a pelvic mass for whom surgery is planned. OVA1 was developed through large pre-clinical studies in collaboration with numerous academic medical centers encompassing over 2,500 clinical samples. OVA1 was fully validated in a prospective multi-center clinical trial encompassing 27 sites reflective of the diverse nature of the clinical centers at which ovarian adnexal masses are evaluated.

In 2012, we completed a second pivotal clinical study of OVA1 called the "OVA500 study," led by Dr. Robert E. Bristow, Director of Gynecologic Oncology Services with University of California Irvine Healthcare. The study evaluated OVA1 diagnostic performance in a population of 494 evaluable patients who underwent surgery for an adnexal mass after enrollment by a non-gynecologic oncologist. In February 2013, the OVA500 study was published in the peer-reviewed journal Gynecologic Oncology, which we believe enjoys the highest impact factor rating of any journal worldwide focused on gynecologic oncology. Since many professional medical societies stress the importance of multiple independent clinical trials as so-called "evidence levels", we also believe that the OVA500 study contributes to a higher evidence level relative to OVA1's utility in the medical management of adnexal masses.

In addition to these pivotal studies, three follow-on studies have been published bringing the number of full research articles on OVA1 clinical performance to a total of five peer-reviewed publications. Together, we believe these data provide strong clinical evidence that OVA1 improves the pre-surgical detection of ovarian cancer, across all stages or subtypes, in patients undergoing surgery for a suspicious ovarian mass.

The American Medical Association Current Procedural Terminology ("CPT®") Panel approved a Category I CPT code (81503) for OVA1, which became effective in January 2013.

Dr. Bristow presented another study at the Society of Gynecological Oncology ("SGO") in March 2013 which was published in the journal Obstetrics & Gynecology (also known as the Green Journal) in June 2013. This study was based on the medical records of 13,321 women with epithelial cancer, the most common type of ovarian cancer, diagnosed from 1999 to 2006 in California. Only 37 percent of these patients received treatment that adhered to guidelines set by the National Comprehensive Cancer Network ("NCCN"), an alliance of 23 major cancer centers with expert panels that analyze, research and recommend cancer treatments. The study found that surgeons who operated on 10 or more women a year for ovarian cancer, and hospitals that treated 20 or more a year, were more likely to adhere to NCCN guidelines and their patients lived longer. Among women with advanced disease — the stage at which ovarian cancer is usually first found — 35 percent survived at least five years if their care met the guidelines, compared with 26 percent of those whose care fell short.

In May 2013, SGO issued a new position statement on OVA1. This second SGO statement on OVA1 since its FDA clearance in 2009 represents another significant step toward acceptance of OVA1 as the standard of care for pre-surgically evaluating the risk of ovarian cancer in women with adnexal masses. The statement, titled "Multiplex Serum Testing for Women with Pelvic Mass", reads:

"Blood levels of five proteins in women with a known ovarian mass have been reported to change when ovarian cancer is present. Tests measuring these proteins may be useful in identifying women who should be referred to a gynecologic oncologist. Recent data have suggested that such tests, along with physician clinical assessment, may improve detection rates of malignancies among women with pelvic masses planning surgery. [1],[2] Results from such tests should not be interpreted independently, nor be used in place of a physician's clinical assessment. Physicians are strongly encouraged to reference the American Congress of Obstetricians and Gynecologists' 2011 Committee Opinion "The Role of the Obstetrician-Gynecologist in the Early Detection of Epithelial Ovarian Cancer" to determine an appropriate care plan for their patients. It is important to note that no such test has been evaluated for use as, nor

cleared by, the FDA as a screening tool for ovarian cancer. SGO does not formally endorse or promote any specific products or brands."

[1] Bristow RE, Smith A, Zhang Z, Chan DW, Crutcher G, Fung ET, et al. Ovarian malignancy risk stratification of the adnexal mass using a multivariate index assay. Gynecol Oncol 2013;128: 252–259

[2] Ueland FR, Desimone CP, Seamon LG, Miller RA, Goodrich S, Podzielinski I, et al. Effectiveness of a multivariate index assay in the preoperative assessment of ovarian tumors. Obstet Gynecol 2011;117:1289-1297.

We believe the position statement does two things:

Lists as references the publications of OVA1's two pivotal clinical studies, comprised of the original FDA validation study published in June 2011 and the OVA500 "intended use" study published in 2013. Together, this offers an extensive, peer-reviewed proof source for physicians and payers to assess OVA1's clinical performance and comparative medical benefits versus today's standard of care.

Places OVA1 use in the context of current American Congress of Obstetricians and Gynecologists ("ACOG") practice guidelines, where CA125 has been used off-label for many years to predict malignancy before surgery, although with inferior performance.

In June 2013 our collaborators from Johns Hopkins Biomarker Discovery and Translation Center presented data from "proof of concept" work to identify markers with high clinical specificity that may complement OVA1. These results were presented in a poster at the annual meeting of the American Society for Clinical Oncology by Dr. Zhen Zhang and co-workers. The study identified a set of 5 biomarkers (CA125II, prealbumin, IGFBP2, IL6 and FSH) which optimally reduced false positives among a targeted set of OVA1-positive benign patients. This panel was subsequently tested in a 50/50 cross-validation strategy against a sampling of OVA500 patients (N=384), to evaluate specificity and other diagnostic parameters. At a fixed sensitivity of 90%, the median specificity of models using the new panel in testing was 80.6%. The mean and median absolute improvements over that of OVA1 were 18.6% and 20.3%, respectively. The new panel demonstrated the possibility to improve specificity over that of the existing OVA1 algorithm, while maintaining a high sensitivity in pre-surgical assessment of malignancy. The work will be submitted for publication in 2014.

We are in the process of identifying intended use(s) and establishing a regulatory or commercial pathway for a potential next-generation OVA product utilizing this or another new panel. Any actual product development will likely differ significantly depending on a number of technical and commercial factors.

A study published in July 2014 in The American Journal of Obstetrics & Gynecology, examined the relationship between two imaging methods, ultrasound and computed tomography, and the OVA1 test result in assessing the risk of ovarian cancer among patients planning surgery for an ovarian mass. Using data obtained from 1,100 ovarian mass surgery patients in two previous pivotal trials of OVA1's clinical performance, conducted in 2007 and 2012, the study found that adding OVA1 reduced the number of ovarian cancers missed with imaging alone by 84-90%. Specifically, ultrasound alone missed 23.1% of ovarian cancers that were presented, but when OVA1 was added in parallel, the number of ovarian cancers missed decreased to 2.2%. When CT was used alone, 20.2% of ovarian cancers were missed but this rate fell to 2.9% when OVA1 was added in parallel. Additionally, the study found that when ultrasound and OVA1 were combined in parallel, 95% of ovarian cancers in a subgroup of early-stage patients were detected.

Novitas Solutions (formerly Highmark Medicare Services), a Medicare contractor, covers and reimburses for OVA1. In December 2013, the Centers for Medicare and Medicaid Services ("CMS") made its final determination and authorized Medicare contractors to set prices for Multianalyte Assays with Algorithmic Analyses ("MAAA") test CPT codes when they determine it is payable. CMS also validated that an algorithm has unique value by specifying that the gap-fill process and not cross-walk should be used by contractors to price MAAA tests. We expect OVA1 to be priced using the gap-fill method. We will be engaged in that process in 2014 for pricing effective January 1, 2015. This decision also sets a precedent for recognizing the value of biomarker developed tests to clinical decision-making and healthcare efficiencies.

Independent BlueCross BlueShield plans representing approximately 8.0 million lives provide coverage for OVA1. In total, including Medicare and other private payers, approximately 55.5 million patients have access to and coverage for OVA1.

Under the terms of our Strategic Alliance Agreement with Quest Diagnostics Incorporated ("Quest Diagnostics"), which we terminated in August 2013, Quest Diagnostics was required to pay us a fixed payment of $50 per OVA1 test performed, as well as 33% of its "gross margin" from revenue from performing OVA1 tests domestically, as that term is defined in the Strategic Alliance Agreement. Prior to the termination of the agreement, Quest Diagnostics had the right to be the exclusive clinical reference laboratory marketplace provider of OVA1 tests in its exclusive territory, which included the US, Mexico, the United Kingdom and India. This right extended through September 11, 2014, and Quest Diagnostics had the right to extend its exclusivity period for an additional year on the same terms and conditions. In August 2013, we sent Quest Diagnostics a notice of termination. Notwithstanding the termination, we agreed that Quest Diagnostics could continue to make OVA1 available to healthcare providers on the same financial terms following the termination while negotiating in good faith towards an alternative business structure. Quest Diagnostics has disputed the effectiveness of our notice of termination.

Corporate Information

We were originally incorporated in 1993, and we had our initial public offering in September 2000. Our executive offices are located at 12117 Bee Caves Road, Building Three, Suite 100, Austin, TX 78759, and our telephone number is (512) 519-0400. We maintain a website at www.vermillion.com and www.aspiralab.com where general information about us is available. Our websites, and the information contained therein, are not a part of this prospectus.

THE OFFERING

Common stock offered by us	Shares of our common stock having an aggregate offering price of up to $15,000,000.
Manner of offering	"At-the-market" offering that may be made from time to time through our sales agent, Cantor Fitzgerald & Co. See "Plan of Distribution" on page S-10.
Use of Proceeds	We currently intend to use the net proceeds from this offering, if any, for general corporate purposes, including capital expenditures and working capital. See "Use of Proceeds" on page S-8 of this at-the-market offering prospectus.
Risk Factors	Investing in our securities involves a high degree of risk. Before making an investment decision, you should read the information contained in or incorporated by reference under the heading "Risk Factors" beginning on page S-6 of this at-the-market offering prospectus, on page 5 of the accompanying base prospectus and in the documents incorporated by reference into this at-the-market offering prospectus.
Nasdaq Capital Market symbol	VRML

The number of shares of our common stock that will be outstanding immediately after this offering as shown above is based on 35,897,776 shares outstanding as of August 31, 2014. The number of shares outstanding as of August 31, 2014, as used throughout this at-the-market offering prospectus, unless otherwise indicated, excludes the following, all as of August 31, 2014:

- 1,796,692 shares of our common stock issuable upon the exercise of outstanding stock options at a weighted average exercise price of $3.59 per share;
- an aggregate of 47,500 shares of our common stock reserved for restricted stock issuances;
-

an aggregate of 952,881 shares of our common stock reserved for future issuance to employees, directors and consultants pursuant to our stock incentive plans; and

- outstanding warrants to purchase an aggregate of 483,359 shares of our common stock at a weighted average exercise price of $1.65 per share.

RISK FACTORS

An investment in our securities involves a high degree of risk. Before deciding whether to invest in our securities, you should consider carefully the risks and uncertainties described below and discussed under the section entitled "Risk Factors" contained in our most recent Annual Report on Form 10-K, any subsequent updates in our Quarterly Reports on Form 10-Q and any other filings we make with the SEC pursuant to Section 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), which are incorporated by reference into this prospectus. The occurrence of any of these risks could materially and adversely affect our business, prospects, financial condition, results of operations or cash flow. Other risks and uncertainties that we do not now consider to be material of which we are not now aware may become important factors that affect us in the future and could result in a complete loss of your investment.

Management will have broad discretion as to the use of the proceeds from this offering and may not use the proceeds effectively.

Because we have not designated the amount of net proceeds from this offering to be used for any particular purpose, our management will have broad discretion as to the application of the net proceeds from this offering and could use them for purposes other than those contemplated at the time of the offering. Our management may use the net proceeds for corporate purposes that may not improve our financial condition or market value.

You may experience dilution.

Since the price per share of our common stock being offered is higher than the net tangible book value per share of our common stock, you will suffer substantial dilution in the net tangible book value of the common stock you purchase in this offering. See the section entitled "Dilution" in this prospectus for a more detailed discussion of the dilution you will incur if you purchase common stock in this offering. In addition, we have a significant number of options outstanding. If the holders of these options exercise such options, you may incur further dilution.

You may experience future dilution as a result of future equity offerings.

To the extent that we raise additional funds through the sale of equity or convertible debt securities, the issuance of such securities will result in dilution to our stockholders. Investors purchasing shares or other securities in the future could have rights superior to existing stockholders. The price per share at which we sell additional shares of our common stock, or securities convertible or exchangeable into common stock, in future transactions may be higher or lower than the price per share paid by investors in this offering.

Sales of a significant number of shares of our common stock in the public markets, or the perception that such sales could occur, could depress the market price of our common stock.

Sales of a substantial number of shares of our common stock in the public markets could depress the market price of our common stock and impair our ability to raise capital through the sale of additional equity securities. We have agreed, without the prior written consent of Cantor Fitzgerald & Co. and subject to certain exceptions set forth in the sales agreement, not to sell or otherwise dispose of any common stock or securities convertible into or exchangeable for shares of common stock, warrants or any rights to purchase or acquire common stock during the period beginning on the fifth trading day immediately prior to the delivery of any placement notice delivered by us to Cantor Fitzgerald & Co. and ending on the fifth trading day immediately following the final settlement date with respect to the shares sold pursuant to such notice. We have further agreed, subject to certain exceptions set forth in the sales agreement, not to sell or otherwise dispose of any common stock or securities convertible into or exchangeable for shares of common stock, warrants or any rights to purchase or acquire our common stock in any other "at-the-market" or

continuous equity transaction prior to the termination of the sales agreement with Cantor Fitzgerald & Co. We cannot predict the effect that future sales of our common stock would have on the market price of our common stock.

The commercialization of our diagnostic tests may be adversely affected by changing FDA regulations, and any delay by or

failure of the FDA to approve our diagnostic tests submitted to the FDA may adversely affect our business, results of

operations and financial condition.

The FDA cleared OVA1 in September 2009. In connection with the clearance of OVA1 we agreed to conduct certain post-market surveillance study to further analyze performance of OVA1 in pre- and post-menopausal women. Failure to comply with our post-marketing study requirements may lead to enforcement actions by FDA, including seizure of our product, injunction, prosecution, and/or civil money penalties, which may irreparably harm our business.

Our activities related to diagnostic products are, or have the potential to be, subject to regulatory oversight by the FDA under provisions of the Federal Food, Drug and Cosmetic Act and regulations thereunder, including regulations governing the development, marketing, labeling, promotion, manufacturing and export of our products. Failure to comply with applicable requirements can lead to sanctions, including withdrawal of products from the market, recalls, refusal to authorize government contracts, product seizures, civil money penalties, injunctions and criminal prosecution.

The Food, Drug and Cosmetic Act requires that medical devices introduced to the United States market, unless exempted by regulation, be the subject of either a pre-market notification clearance, known as a 510(k) clearance or 510(k) de novo clearance, or a pre-market approval (“PMA”). Some of our potential future clinical products may require a 510(k) or 510(k) de novo clearance, while

others may require a PMA. With respect to devices reviewed through the 510(k) process, we may not market a device until an order is issued by the FDA finding our product to be substantially equivalent to a legally marketed device known as a predicate device. A 510(k) submission may involve the presentation of a substantial volume of data, including clinical data. The FDA may agree that the product is substantially equivalent to a predicate device and allow the product to be marketed in the United States. On the other hand, the FDA may determine that the device is not substantially equivalent and require a PMA, or require further information, such as additional test data, including data from clinical studies, before it is able to make a determination regarding substantial equivalence. By requesting additional information, the FDA can delay market introduction of our products. Delays in receipt of or failure to receive any necessary 510(k) clearance or PMA approval, or the imposition of stringent restrictions on the labeling and sales of our products, could have a material adverse effect on our business, results of operations and financial condition. If the FDA indicates that a PMA is required for any of our potential future clinical products, the application will require extensive clinical studies, manufacturing information and likely review by a panel of experts outside the FDA. Clinical studies to support either a 510(k) submission or a PMA application would need to be conducted in accordance with FDA requirements. Failure to comply with FDA requirements could result in the FDA’s refusal to accept the data or the imposition of regulatory sanctions. We cannot assure that any necessary 510(k) clearance or PMA approval will be granted on a timely basis, or at all. To the extent we seek FDA 510(k) clearance or FDA pre-market approval for other diagnostic tests, any delay by or failure of the FDA to clear or approve those diagnostic tests may adversely affect our consolidated revenues, results of operations and financial condition.

FORWARD-LOOKING STATEMENTS

This at-the-market offering prospectus, the accompanying base prospectus, the documents we have filed with the SEC that are incorporated by reference and any free writing prospectus that we have authorized for use in connection with this offering contain "forward-looking statements" within the meaning of Section 27A of the Securities Act and Section 21E of the Securities Exchange Act of 1934, as amended (the "Exchange Act"). These statements involve a number of risks and uncertainties that are difficult to predict. In some cases, you can identify forward-looking statements by words such as "may," "expects," "intends," "anticipates," "believes," "estimates," "plans," "seeks," "could," "sh "continue," "will," "potential," "projects" or other similar expressions. Readers are cautioned that these forward-looking statements speak only as of the date on which the document in which they appear is filed with the SEC, and we do not assume any obligation to update, amend or clarify them to reflect events, new information or circumstances after such dates. Forward-looking statements are subject to risks, uncertainties and assumptions that are difficult to predict.

You should read this at-the-market offering prospectus, the accompanying base prospectus, any related free writing prospectus and the documents that we reference herein and therein and have filed as exhibits to the registration statement, of which this prospectus is part, completely and with the understanding that our actual future results may be materially different from what we currently expect. You should not put undue reliance on any forward-looking statement. We believe it is important to communicate our expectations to our investors. However, there may be events in the future that we are not able to accurately predict or that we do not fully control that could cause actual results to differ materially from those expressed or implied in our forward-looking statements.

USE OF PROCEEDS

We currently intend to use the net proceeds from this offering, if any, for general corporate purposes, including working capital, for further research and development and ongoing sales and marketing expenses, and, potentially, capital expenditures and licensing of additional technologies. We may also use a portion of the net proceeds from this offering to acquire or invest in complementary businesses, technologies, product candidates or other intellectual property, although we have no present commitments or agreements to do so. The amount of the proceeds from this offering will depend upon the number of shares of our common stock sold and the market price at which they are sold. There can be no assurance that we will sell any shares under or fully utilize the sales agreement with Cantor as a source of financing.

As of the date of this at-the-market offering prospectus, we cannot specify with certainty all of the particular uses for the net proceeds to us from this offering. As a result, our management will have broad discretion regarding the timing and application of the net proceeds from this offering. Pending the uses described above, we intend to invest the net proceeds in interest-bearing, investment-grade securities.

DILUTION

If you invest in our common stock, your interest will be diluted immediately to the extent of the difference between the public offering price per share of our common stock and the as-adjusted net tangible book value per share of common stock after this offering.

The net tangible book value of our common stock as of June 30, 2014 was approximately $17,742,000, or approximately $0.49 per share. Net tangible book value per share represents the amount of our total tangible assets less total liabilities divided by the total number of shares of our common stock outstanding.

Dilution per share to new investors represents the difference between the amount per share paid by purchasers for our common stock in this offering and the net tangible book value per share of our common stock immediately following the completion of this offering.

After giving effect to the sale of shares of common stock offered by this prospectus at an assumed public offering price of $2.21 per share (the last reported sale price of our common stock on The NASDAQ Capital Market on September 11, 2014) and after deducting commissions and estimated aggregate offering expenses payable by us), our as adjusted net tangible book value as of June 30, 2014 would have been approximately $32,117,000, or approximately $0.75 per share. This represents an immediate increase in net tangible book value of approximately $0.26 per share to our existing stockholders and an immediate dilution in as adjusted net tangible book value of approximately $1.46 per share to purchasers of our common stock in this offering, as illustrated by the following table:

.49.

assumed public offering price per share		$ 2.21
Net tangible book value per share as of June 30, 2014	$ 0.49	
Increase in net tangible book value per share attributable to this offering	0.26	
As adjusted net tangible book value per share as of June 30, 2014, after giving effect to this offering		$ 0.75
Dilution per share to new investors purchasing shares in this offering		$ 1.46

The above table assumes for illustrative purposes that an aggregate of 6,787,330 shares of our common stock are sold at a price of $2.21 per share, the last reported sale price of our common stock on The NASDAQ Capital Market on September 11, 2014, for aggregate gross proceeds of approximately $15,000,000. The shares sold in this offering, if any, will be sold from time to time at various prices. An increase of $1.00 per share in the price at which the shares are sold from the assumed offering price of $2.21 per share shown in the table above, assuming all of our common stock in the aggregate amount of $15,000,000 is sold at that price, would increase our as adjusted net tangible book value per share after the offering to $0.91 per share and would increase the dilution in net tangible book value per share to new investors to $2.30 per share, after deducting commissions and estimated aggregate offering expenses payable by us. A decrease of $1.00 per share in the price at which the shares are sold from the assumed offering price of $2.21 per share shown in the table above, assuming all of our common stock in the aggregate amount of $15,000,000 is sold at that price, would decrease our as adjusted net tangible book value per share after the offering to $0.60 per share and would decrease the dilution in net tangible book value per share to new investors to $0.61 per share, after deducting commissions and estimated aggregate offering expenses payable by us.

The information discussed above is illustrative only and will adjust based on the actual public offering prices and other terms of this offering. The above table is based on 35,897,776 shares outstanding as of August 31, 2014 and excludes as of such date:

- 1,796,692 shares of our common stock issuable upon the exercise of outstanding stock options at a weighted average exercise price of $3.59 per share;
- an aggregate of 47,500 shares of our common stock reserved for restricted stock issuances;
- an aggregate of 952,881 shares of our common stock reserved for future issuance to employees, directors and consultants pursuant to our stock incentive plans; and
- outstanding warrants to purchase an aggregate of 483,359 shares of our common stock at a weighted average exercise price of $1.65 per share.

To the extent that outstanding options are exercised, you will experience further dilution. In addition, we may choose to raise additional capital due to market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. To the extent that additional capital is raised through the sale of equity or convertible debt securities, the issuance of these securities could result in further dilution to our stockholders.

PLAN OF DISTRIBUTION

We have entered into a Controlled Equity OfferingSM Sales Agreement (the "sales agreement") with Cantor Fitzgerald & Co. ("Cantor") under which we may issue and sell shares of our common stock at an aggregate purchase price of up to $15,000,000 from time to time through Cantor acting as agent. The sales agreement has been filed as an exhibit to our registration statement on Form S-3 of which this at-the-market offering prospectus forms a part. Cantor may sell the common stock by any method that is deemed to be an "at-the-market" equity offering as defined in Rule 415 promulgated under the Securities Act, including sales made directly on or through The NASDAQ Capital Market or any other existing trading market for the common stock in the United States or to or through a market maker. Cantor may also sell our common stock in privately negotiated transactions, subject to our prior approval. Upon delivery of a placement notice and subject to the terms and conditions of the sales agreement, Cantor may sell our common stock by any method permitted by law deemed to be an "at-the-market" offering as defined in Rule 415 promulgated under the Securities Act, including sales made directly on The NASDAQ Capital Market, on any other existing trading market for our common stock or to or through a market maker. Cantor may also sell our common stock by any other method permitted by law, including in privately negotiated transactions. We may instruct Cantor not to sell common stock if the sales cannot be effected at or above the price designated by us from time to time. We or Cantor may suspend the offering of common stock upon notice and subject to other conditions.

We will pay Cantor commissions, in cash, for its services in acting as agent in the sale of our common stock. Cantor will be entitled to compensation at a fixed commission rate of up to 3.0% of the gross sales price per share sold. Because there is no minimum offering amount required as a condition to close this offering, the actual total public offering amount, commissions and proceeds to us, if any, are not determinable at this time. We have also agreed to reimburse Cantor for certain specified expenses, including the fees and disbursements of its legal counsel in an amount not to exceed $50,000. We estimate that the total expenses for the offering, excluding compensation and reimbursements payable to Cantor under the terms of the sales agreement, will be approximately $175,000.

Settlement for sales of common stock will occur on the third business day following the date on which any sales are made, or on some other date that is agreed upon by us and Cantor in connection with a particular transaction, in return for payment of the net proceeds to us. Sales of our common stock as contemplated in the prospectus will be settled through the facilities of the Depository Trust Company or by such other means upon which we and Cantor may agree. There is no arrangement for funds to be received in an escrow, trust or similar arrangement.

Cantor will use its commercially reasonable efforts, consistent with its sales and trading practices, to solicit offers to purchase our common stock under the terms and subject to the conditions set forth in the sales agreement. In connection with the sale of the common stock on our behalf, Cantor will be deemed to be an "underwriter" within the meaning of the Securities Act and the compensation of Cantor will be deemed to be underwriting commissions or discounts. We have agreed to provide indemnification and contribution to Cantor against certain civil liabilities, including liabilities under the Securities Act.

The offering of our common stock pursuant to the sales agreement will terminate upon the earlier of (1) the sale of all shares of our common stock subject to the sales agreement having an aggregate offering price of $15,000,000, or (2) termination of the sales agreement as permitted therein. We and Cantor may each terminate the sales agreement at any time upon ten days' prior notice.

Cantor and its affiliates may in the future provide various investment banking, commercial banking and other financial services to us and our affiliates, for which services they may in the future receive customary fees. To the extent required by Regulation M under the Exchange Act, Cantor will not engage in any market making activities involving our common stock while the offering is ongoing under this at-the-market offering prospectus.

This at-the-market offering prospectus in electronic format may be made available on a website maintained by Cantor, and Cantor may distribute this at-the-market offering prospectus and the accompanying base prospectus electronically.

On May 8, 2013, we entered into a securities purchase agreement in connection with a private placement, pursuant to which certain existing and new investors (the "Purchasers") agreed to purchase shares of our common stock and warrants to purchase shares of our common stock. In connection with the private placement, on May 13, 2013, we entered into a stockholders agreement (the "Stockholders Agreement") with certain of the Purchasers. Among other things, the Stockholders Agreement provides certain of the Purchasers with the rights to participate in any future equity offerings by us on the same price and terms as other investors. As a result, unless the Purchasers waive their rights under the Stockholders Agreement, we will be required to offer such Purchasers the right to participate in this Offering pursuant to the terms of the Stockholders Agreement.

LEGAL MATTERS

The validity of the securities offered by this prospectus will be passed upon by Sidley Austin LLP. Cantor is being represented in connection with this offering by Reed Smith LLP, New York, New York.

EXPERTS

The consolidated financial statements as of December 31, 2013 and 2012 and for the years then ended incorporated by reference in this prospectus have been so incorporated in reliance on the report of BDO USA, LLP, an independent registered public accounting firm, incorporated herein by reference, given on the authority of said firm as experts in auditing and accounting.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and current reports, proxy statements and other information with the SEC. We have filed with the SEC a registration statement on Form S-3 under the Securities Act with respect to the securities we are offering under this prospectus. This prospectus does not contain all of the information set forth in the registration statement and the exhibits to the registration statement. For further information with respect to us and the securities we are offering under this prospectus, we refer you to the registration statement and the exhibits and schedules filed as a part of the registration statement. You may read and copy the registration statement, as well as our reports, proxy statements and other information, at the SEC's Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for more information about the operation of the Public Reference Room. The SEC maintains an Internet site that contains reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC, including Vermillion, Inc. The SEC's Internet site can be found at http://www.sec.gov.

Information on any Vermillion website, any subsection, page, or other subdivision of any Vermillion website, or any website linked to by content on any Vermillion website, is not part of this prospectus and you should not rely on that information unless that information is also in this prospectus or incorporated by reference in this prospectus.

IMPORTANT INFORMATION INCORPORATED BY REFERENCE

The SEC allows us to "incorporate by reference" information into this prospectus, which means that we can disclose important information to you by referring you to another document filed separately with the SEC. The documents incorporated by reference into this prospectus contain important information that you should read about us.

The following documents are incorporated by reference into this prospectus:

(a) Our Annual Report on Form 10-K for the fiscal year ended December 31, 2013 filed with the SEC on March 31, 2014;
(b) Our Quarterly Report on Form 10-Q for the quarters ended March 31, 2014 and June 30, 2014 filed with the SEC on May 15, 2014 and August 14, 2014, respectively;
(c) Our Current Reports on Form 8-K filed with the SEC on (i) January 3, 2014, (ii) March 10, 2014, (iii) March 31, 2014, (iv) April 15, 2014, (v) April 18, 2014, (vi) April 23, 2014, (vii) June 24, 2014, (vii) July 28, 2014, (ix) August 15, 2014 and (x) August 21, 2014;
(d) The description of our common stock set forth in the Registration Statement on Form S-1 filed with the SEC on February 21, 2011 (File No. 333-171797), including any amendments or reports filed for the purpose of updating such description.

We also incorporate by reference any future filings (other than current reports furnished under Item 2.02 or Item 7.01 of Form 8-K and exhibits filed on such form that are related to such items unless such Form 8-K expressly provides to the contrary) made with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act, including those

made after the date of the initial filing of the registration statement of which this prospectus is a part and prior to effectiveness of such registration statement, until we file a post-effective amendment that indicates the termination of the offering of the securities made by this prospectus and will become a part of this prospectus from the respective dates that such documents are filed with the SEC. Any statement contained herein or in a document incorporated or deemed to be incorporated by reference herein shall be deemed to be modified or superseded for purposes hereof or of the related prospectus supplement to the extent that a statement contained herein or in any other subsequently filed document which is also incorporated or deemed to be incorporated herein modifies or supersedes such statement. Any such statement so modified or superseded shall not be deemed, except as so modified or superseded, to constitute a part of this prospectus.

We will furnish without charge to you, upon written or oral request, a copy of any or all of the documents incorporated by reference, including exhibits to these documents, by writing or telephoning us at the following address:

Vermillion, Inc.

12117 Bee Caves Road, Building Three, Suite 100

Austin, Texas 78738

(512) 519-0400

Attn: Corporate Secretary

S-12

Up to $15,000,000 of Shares

Common Stock

PROSPECTUS

, 2014

PART II

INFORMATION NOT REQUIRED IN PROSPECTUS

Item 14. Other Expenses of Issuance and Distribution

The following table sets forth the estimated costs and expenses, other than underwriting discounts and commissions payable by us in connection with the offering of the securities being registered. All the amounts shown are estimates, except for the SEC registration fee and the FINRA filing fee:

SEC Registration Fee	$ 6,440
FINRA Filing Fee	8,000
Legal Fees and Expenses	130,000
Accounting Fees and Expenses	20,000
Miscellaneous	10,560
Total	$ 175,000

Item 15. Indemnification of Directors and Officers

Under Section 145 of the DGCL, a corporation may indemnify any person who was or is a party or is threatened to be made a party to any threatened, pending or completed action, suit or proceeding, whether civil, criminal, administrative or investigative (other than an action by or in the right of the corporation) by reason of the fact that he is or was a director, officer, employee or agent of the corporation, or is or was serving at the request of the corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise, against expenses (including attorney's fees), judgments, fines and amounts paid in settlement actually and reasonably incurred by such person in connection with such action, suit or proceeding (i) if such person acted in good faith and in a manner that the person reasonably believed to be in or not opposed to the best interests of the corporation and (ii) with respect to any criminal action or proceeding, if he had no reasonable cause to believe such conduct was unlawful. In actions brought by or in the right of the corporation, a corporation may indemnify such person against expenses (including attorney's fees) actually and reasonably incurred by such person in connection with the defense or settlement of such action or suit if such person acted in good faith and in a manner that the person reasonably believed to be in or not opposed to the best interests of the corporation, except that no indemnification may be made in respect of any claim, issue or matter as to which that person has been adjudged to be liable to the corporation unless and only to the extent that the Court of Chancery of the State of Delaware or the court in which such action or suit was brought determines upon application that, despite the adjudication of liability but in view of all circumstances of the case, such person is fairly and reasonably entitled to indemnification for such expense which the Court of Chancery or other such court deems proper. To the extent that such person has been successful on the merits or otherwise in defending any such action, suit or proceeding referred to above in any claim, issue or matter therein, he is entitled to indemnification for expenses (including attorney's fees) actually and reasonably incurred by him in connection therewith. The indemnification and advancement of expenses provided for or granted pursuant to Section 145 of the DGCL are not exclusive of any other rights of indemnification or advancement of expenses to which those seeking indemnification or advancement of expenses may be entitled, and a corporation may purchase and maintain insurance against liabilities asserted against any former or current director, officer, employee or agent of the corporation, or a person who is or was serving at the request of the corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise, whether or not the power to indemnify is provided by the statute.

Section 102(b)(7) of the DGCL permits a corporation to provide in its certificate of incorporation that a director of the corporation shall not be personally liable to the corporation or its stockholders for monetary damages for breach of fiduciary duty as a director, except for liability for any breach of the director's duty of loyalty to the corporation or its stockholders, for acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of the law, for unlawful payments of dividends or unlawful stock repurchases, redemptions or other distributions, or for any transaction from which the director derived an improper personal benefit. Article VII of our Certificate of Incorporation provides for such limitation of liability.

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers or persons controlling our company pursuant to the foregoing provisions, we have been informed that in the opinion of the SEC such indemnification is against public policy as expressed in the Act and is therefore unenforceable.

Certificate of Incorporation and Bylaws. Article VII of our Certificate of Incorporation and Article VI of our Bylaws provide in substance that, to the fullest extent permitted by the DGCL, each director and officer shall be indemnified against reasonable costs and expenses, including attorneys' fees, and any liabilities which he may incur in connection with any action to which he may be made a party by reason of his being or having been a director or officer of our company, a predecessor of our company, or serves or served as a director, officer or employee of another enterprise at the request of our company or any predecessor of our company. The indemnification provided by our Certificate of Incorporation is not deemed exclusive of or intended in any way to limit any other rights to which any person seeking indemnification may be entitled.

D&O Insurance. We maintain standard policies of insurance under which coverage is provided to our directors and officers against loss arising from claims made by reason of breach of duty or other wrongful act, and to us with respect to payments which may be made by us to such officers and directors pursuant to the above indemnification provision or otherwise as a matter of law.

Item 16. Exhibit

The exhibits listed in the exhibit index immediately following the signature pages are filed as part of this registration statement.

Item 17. Undertakings

The undersigned registrant hereby undertakes:

(1) To file, during any period in which offers or sales are being made, a post-effective amendment to this registration statement:

(i) To include any prospectus required by Section 10(a)(3) of the Securities Act of 1933;

(ii) To reflect in the prospectus any facts or events arising after the effective date of the registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the registration statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the Commission pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than a 20 percent change in the maximum aggregate offering price set forth in the "Calculation of Registration Fee" table in the effective registration statement.

(iii) To include any material information with respect to the plan of distribution not previously disclosed in the registration statement or any material change to such information in the registration statement;

Provided, however, that:

Paragraphs (1)(i), (1)(ii) and (1)(iii) of this section do not apply if the information required to be included in a post-effective amendment by those paragraphs is contained in reports filed with or furnished to the Commission by the registrant pursuant to Section 13 or Section 15(d) of the Securities Exchange Act of 1934 that are incorporated by reference in the registration statement, or is contained in a form of prospectus filed pursuant to Rule 424(b) that is part of the registration statement.

(2) That, for the purpose of determining any liability under the Securities Act of 1933, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

(3) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.

(4) That, for the purpose of determining liability under the Securities Act of 1933 to any purchaser:

(i) Each prospectus filed by the registrant pursuant to Rule 424(b)(3) shall be deemed to be part of the registration statement as of the date the filed prospectus was deemed part of and included in the registration statement; and

(ii) Each prospectus required to be filed pursuant to Rule 424(b)(2), (b)(5), or (b)(7) as part of a registration statement in reliance on Rule 430B relating to an offering made pursuant to Rule 415(a)(1)(i), (vii), or (x) for the purpose of providing the information required by Section 10(a) of the Securities Act of 1933 shall be deemed to be part of and included in the registration statement as of the earlier of the date such form of prospectus is first used after effectiveness or the date of the first contract of sale of securities in the offering described in the prospectus. As provided in Rule 430B, for liability purposes of the issuer and any person that is at that date an underwriter, such date shall be deemed to be a new effective date of the registration statement relating to the securities in the registration statement to which that prospectus relates, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof. Provided, however, that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated by reference into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such effective date, supersede or modify any statement that was made in the registration statement or prospectus that was part of the registration statement or made in any such document immediately prior to such effective date.

(5) That, for the purpose of determining liability of the registrant under the Securities Act of 1933 to any purchaser in the initial distribution of the securities: The undersigned registrant undertakes that in a primary offering of the securities of the undersigned registrant pursuant to this registration statement, regardless of the underwriting method used to sell the securities to the purchaser, if the securities are offered or sold to such purchaser by means of any of the following communications, the undersigned registrant will be a seller to the purchaser and will be considered to offer or sell such securities to such purchaser:

(i) Any preliminary prospectus or prospectus of the undersigned registrant relating to the offering required to be filed pursuant to Rule 424;

(ii) Any free writing prospectus relating to the offering prepared by or on behalf of the undersigned registrant or used or referred to by the undersigned registrant;

(iii) The portion of any other free writing prospectus relating to the offering containing material information about the undersigned registrant or its securities provided by or on behalf of the undersigned registrant; and

(iv) Any other communication that is an offer in the offering made by the undersigned registrant to the purchaser.

(6) That, for purposes of determining any liability under the Securities Act of 1933, each filing of the registrant's annual report pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934 (and, where applicable, each filing of an employee benefit plan's annual report pursuant to Section 15(d) of the Securities Exchange Act of 1934) that is incorporated by reference in the registration statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

(7) Insofar as indemnification for liabilities arising under the Securities Act of 1933 may be permitted to directors, officers and controlling persons of the registrant pursuant to the foregoing provisions, or otherwise, the registrant has been advised that in the opinion of the Commission such indemnification is against public policy as expressed in the Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Act and will be governed by the final adjudication of such issue.

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, the registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and has duly caused this registration statement to be signed on its behalf by the undersigned, thereunto duly authorized in the city of Austin, State of Texas, on September 12, 2014.

Vermillion, Inc.

By: /s/ James T. Lafrance

James T. LaFrance

President and Chief Executive Officer

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints James T. LaFrance and Eric J. Schoen, and each or any one of them, his true and lawful attorney-in-fact and agent, with full power of substitution and resubstitution, for him and in his name, place and stead, in any and all capacities, to sign any and all amendments (including post-effective amendments), and any registration statement for the same offering that is to be effective under Rule 462(b) of the Securities Act, to this registration statement, and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith, as fully to all intents and purposes as he might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents, or any of them, or their or his substitutes or substitute, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act of 1933, this registration statement has been signed by the following persons in the capacities and on the dates indicated.

Signature	Title	Date
/s/ James T. LaFrance	President and Chief Executive Officer	September 12, 2014
James T. LaFrance		

	(Principal Executive Officer) and Chairman of the Board	
/s/ Eric J. Schoen Eric J. Schoen	Vice President, Finance and Chief Accounting Officer (Principal Financial and Accounting Officer)	September 12, 2014
/s/ James S. Burns James S. Burns	Director	September 12, 2014
/s/ Peter S. Roddy Peter S. Roddy	Director	September 12, 2014
/s/ Carl Severinghaus Carl Severinghaus	Director	September 12, 2014
/s/ Robert Goggin Robert Goggin	Director	September 12, 2014
/s/ Eric Varma Eric Varma	Director	September 12, 2014

Exhibit Index

Exhibit Number	Exhibit Description	Incorporated by Reference Form	File No.	Exhibit	Filing Date	Filed Herewith
1.1	Sales Agreement, dated September 12, 2014, by and between Vermillion, Inc. and Cantor Fitzgerald & Co.					
4.1	Fourth Amended and Restated Certificate of Incorporation of Vermillion, Inc. dated January 22, 2010	8-K	000-31617	3.1	January 25, 2010	
4.2	Fifth Amended and Restated Bylaws of Vermillion, Inc., as amended effective June 19, 2014	8-K	000-34810	3.2	August 14, 2014	
4.3	Form of Vermillion, Inc. (formerly Ciphergen Biosystems, Inc.) Common Stock Certificate	S-1/A	333-32812	4.1	August 24, 2000	
4.4	Form of Vermillion, Inc. Warrant, issued May 13, 2013					
4.5	Vermillion, Inc. Common Stock Purchase Warrant to Liolios Group, Inc., issued November 1, 2012					
4.6	Vermillion, Inc. Common Stock Purchase Warrant to Liolios Group, Inc., issued May 1, 2013					
4.7	Vermillion, Inc. Common Stock Purchase Warrant to Liolios Group, Inc., issued November 1, 2013					
4.8	Vermillion, Inc. Common Stock Purchase Warrant to Liolios Group, Inc., issued May 1, 2014					
5.1	Opinion of Sidley Austin LLP					(1)
23.1	Consent of BDO USA, LLP, Independent Registered Public Accounting Firm					
24.1	Power of Attorney					(2)

(1) To be filed by amendment to this registration statement.

(2) Contained herein on the signature page.