

PACIFIC BIOSCIENCES OF CALIFORNIA, INC.
Form 10-K
March 12, 2015

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

Form 10-K

(Mark One)

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

For the fiscal year ended December 31, 2014

Or

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

For the transition period from _____ to _____

Commission File Number 001-34899

Pacific Biosciences of California, Inc.

(Exact name of registrant as specified in its charter)

Delaware
(State or other jurisdiction of
incorporation or organization)

16-1590339
(I.R.S. Employer
Identification No.)

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1380 Willow Road

Menlo Park, CA 94025 94025
(Address of principal executive offices) (Zip Code)

(Registrant's telephone number, including area code)

(650) 521-8000

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

Title of Each Class	Name of Each Exchange on Which Registered
Common Stock, par value \$0.001 per share	The NASDAQ Stock Market LLC

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

None

Indicate by check mark if the registrant is a well-known, seasoned issuer, as defined in Rule 405 of the Securities Act. Yes No

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes No

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes No

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes No

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K.

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

Large accelerated filer

Accelerated filer

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

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

Aggregate market value of registrant's common stock held by non-affiliates of the registrant on June 30, 2014, based upon the closing price of Common Stock on such date as reported by NASDAQ Global Select Market, was approximately \$315,556,000. Shares of voting stock held by each officer and director have been excluded in that such persons may be deemed to be affiliates. This assumption regarding affiliate status is not necessarily a conclusive determination for other purposes.

Number of shares outstanding of the issuer's common stock as of March 3, 2015: 74,516,357

DOCUMENTS INCORPORATED BY REFERENCE:

Portions of the registrant's definitive Proxy Statement relating to its 2015 Annual Meeting of Stockholders to be held on May 20, 2015 are incorporated by reference into Part III of this Form 10-K where indicated. Such Proxy Statement will be filed with the U.S. Securities and Exchange Commission within 120 days after the end of the fiscal year to which this report relates.

Pacific Biosciences of California, Inc.

Annual Report on Form 10-K

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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

Discussions under the captions “Business”, “Risk Factors,” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations,” contain or may contain forward-looking statements that are based on the beliefs and assumptions of the management of Pacific Biosciences of California, Inc. (the “Company,” “we,” “us,” or “our,”) and on information currently available to our management. The statements contained in this Annual Report on Form 10-K that are not purely historical are forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended (the “Exchange Act”), and include, but are not limited to, our statements regarding the sequencing advantages of SMRT® technology, current and future products, market opportunities, strategic plans, expectations regarding the conversion of backlog to revenue, expectations regarding our collaboration agreements including expected revenue and related milestone payments, manufacturing plans, research and development plans, product development, competition, expectations regarding unrecognized income tax benefits, expectations regarding the impact of an increase in market rates on the value of our financial instruments, the sufficiency of cash, cash equivalents and investments to fund projected operating requirements, and the effects of recent accounting pronouncements on our financial statements. Such statements may be signified by terms such as “anticipates,” “believes,” “could,” “estimates,” “expects,” “intends,” “may,” “plan,” “potential,” “predicts,” “projects,” “seeks,” “should,” “target,” “will,” “would” or similar expressions and the negatives of those terms. Forward-looking statements involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. Factors that could cause or contribute to such differences include, but are not limited to, those discussed under the heading “Risk Factors” in this report and in other documents we file with the Securities and Exchange Commission (“SEC”). Given these risks and uncertainties, you should not place undue reliance on forward-looking statements. Also, forward-looking statements represent management’s beliefs and assumptions as of the date of this report. We assume no obligation to update forward-looking statements publicly, or to update the reasons actual results could differ materially from those anticipated in these forward-looking statements, even if new information becomes available in the future.

ITEM 1. BUSINESS

Overview

We design, develop and manufacture the PacBio® RS II Sequencing System to help scientists resolve genetically complex problems. Based on our novel Single Molecule, Real-Time (SMRT®) technology, our products enable: de novo genome assembly to finish genomes in order to more fully identify, annotate and decipher genomic structures; full-length transcript analysis to improve annotations in reference genomes, characterize alternatively spliced isoforms and find novel genes; targeted sequencing to more comprehensively characterize genetic variations; and DNA base modification identification to help characterize epigenetic regulation and DNA damage. Our technology combines very high consensus accuracy and long read lengths with the ability to detect real-time kinetic information.

Our customers and our scientific collaborators have published a number of peer-reviewed articles in journals including Nature, Science, Cell, PNAS and The New England Journal of Medicine highlighting the power and applications of the SMRT platform in projects such as finishing genomes, structural variation discovery, isoform transcriptome characterization, rare mutation discovery and the identification of chemical modifications of DNA related to virulence and pathogenicity. Our research and development efforts are focused on seeking to further improve our existing products, including continuing chemistry and sample preparation improvements to increase throughput and expand our supported applications, and developing new products. By providing access to genetic information that was previously inaccessible, Pacific Biosciences enables scientists to confidently increase their understanding of biological systems.

Pacific Biosciences of California, Inc., formerly Nanofluidics, Inc. was incorporated in the State of Delaware in 2000. Our executive offices are located at 1380 Willow Road, Menlo Park, California 94025, and our telephone number is (650) 521-8000.

The Underlying Science

Genetic inheritance in living systems is conveyed through a naturally occurring information storage system known as deoxyribonucleic acid, or DNA. DNA stores information in linear chains of the chemical bases adenine, cytosine, guanine and thymine, represented by the symbols, A, C, G and T. Inside living cells, these chains usually exist in pairs bound together in a double helix by complementary bases, with A of one strand always binding to a T of the other strand and C always binding to G.

In humans, there are approximately three billion DNA base-pairs in the molecular blueprint of life, called the genome. These three billion bases are divided into 23 chromosomes ranging in size from 50 million to 250 million bases. Normally, there are two complete copies of the genome contained in each cell, one of maternal origin and the other of paternal origin. When cells divide, the genomes are replicated by an enzyme called DNA polymerase, which visits each base in the sequence, creating a complementary copy of each chromosome using building blocks called nucleotides. Contained within these chromosomes are approximately 23,000 smaller regions, called genes, each one containing the recipe for a protein or group of related proteins. The natural process of protein production takes place in steps. In a simplified model, the first step is transcription, a process in which an enzyme called RNA polymerase uses DNA as a template to synthesize new strands of messenger RNA, or mRNA. The mRNAs are then translated into

proteins by ribosomes. The resulting proteins go on to play crucial roles in cellular structure and function and thus the operation of biological systems.

Numerous scientific approaches have evolved to adapt to the emerging awareness of the magnitude of complexity embedded in biological systems. The field of genomics developed to study the interactions among components in the genome and the massive quantities of associated data. Subsequently, proteomics, transcriptomics and a number of other related fields emerged.

Advances in biology over the next decade are expected to be shaped by a more detailed understanding of the fundamental complexity of biological systems. These systems vary among individuals in previously unrecognized ways and are influenced by factors including time, molecular interactions, and cell type.

Importantly for the future of genomics, the first few whole-genome sequencing studies of disease have shown that rare mutations play a critical role in human disease. These mutations would not have been detected in earlier studies because too few people, or perhaps only one person, carry the specific mutation. In addition, it is now understood that structural changes to the genome in which whole sections are deleted, inverted, copied or moved may be responsible for a significant fraction of variation among individuals. The scope of these structural changes challenges the very idea of a reference genome.

Recent discoveries have highlighted additional complexities in the building blocks of DNA and RNA, including the presence of modified bases. It has long been known that in humans and many other multicellular organisms, the cytosine bases can be chemically modified through the addition of a methyl group in a process called methylation. These chemical modifications have been shown to play a role in embryonic development, have important impacts on diseases such as cancer and can even affect the characteristics of offspring for multiple generations. More recently, it has been discovered that other modified bases, such as 5-hydroxymethylcytosine, or hmC, 8-oxoguanine and many others, play important physiological roles. For example, in bacteria, N6-methyladenine has been shown to play an important role in pathogenicity.

Another source of complexity derives from the processing of RNA molecules after being transcribed from the genome. The majority of all genes code for different forms of a protein that can be made depending on the structure of the RNA molecule, referred to as splice variants. A detailed understanding of both the expression pattern and regulation of these variants is believed to play an important role in a number of critical biological processes.

Recent advances in our understanding of biological complexity have highlighted the need for advanced tools such as the PacBio RS II to study DNA, RNA and proteins. In the field of DNA sequencing, incremental technological advances have provided novel insights into the structure and function of the genome. Despite these advances, researchers have not been able to fully characterize the human genome and the genomes of other living organisms because of inherent limitations in these tools.

Evolution of Sequencing

In order to understand the limitations of current DNA sequencing technologies, it is important to understand the sequencing process. This consists of three phases: sample preparation, physical sequencing, and analysis. The first step of sample preparation is to either break the target genome into multiple small fragments or, depending on the amount of sample DNA available, amplify the target region using a variety of molecular methods. In the physical sequencing phase, the individual bases in each fragment are identified in order, creating individual reads. The number of individual bases identified contiguously is defined as read length. In the analysis phase, bioinformatics software is used to align overlapping reads, which allows the original genome to be assembled into contiguous sequence. The longer the read length, the easier it is to assemble the genome.

First Generation Sequencing

First generation sequencing, often referred to as “Sanger sequencing,” was originally developed by Frederick Sanger in 1977. With this technology, during sample preparation, scientists first make different sized fragments of DNA each starting from the same location. Each fragment ends with a particular base that is labeled with one of four fluorescent dyes corresponding to that particular base. Then all of the fragments are distributed in order of their length by driving them through a gel. Information regarding the last base is used to determine the original sequence. Under standard conditions, this method results in a read length that is approximately 700 bases on average, but may be extended to 1,000 bases. These are relatively long read lengths compared with many other sequencing methods. However, first generation sequencing is limited by the small amounts of data that can be processed per unit of time, referred to as throughput.

Second Generation Sequencing

Commercial second generation DNA sequencing tools emerged in 2005 in response to the low throughput of first generation methods. To address this problem, second generation sequencing tools, also commonly referred to as “next generation sequencing”, achieve much higher throughput by sequencing a large number of DNA molecules in parallel. In order to generate this large number of DNA molecules, a copying method called PCR amplification is required. In addition to adding time and complexity to the sample preparation process, the amplification process can introduce errors known as amplification bias. The effect of this bias is resulting copies are not uniformly representative of the original template DNA. In cases where the original template DNA contains regions of relatively high G-C content or relatively high A-T content, the PCR amplification process tends to under-represent these regions. As a result, these regions, which may contain entire genes, can be completely missed in the process.

In most second generation tools, tens of thousands of identical strands are anchored to a given location to be read in a process consisting of successive flushing and scanning operations. The “flush and scan” sequencing process involves sequentially flushing in reagents, such as labeled nucleotides, incorporating nucleotides into the DNA strands,

stopping the incorporation reaction, washing out the excess reagent, scanning to identify the incorporated base and finally treating that base so that the strand is ready for the next “flush and scan” cycle. This cycle is repeated until the reaction is no longer viable.

Due to the large number of flushing, scanning and washing cycles required, the time to result for second generation methods is generally long, often taking days. This repetitive process also limits the average read length produced by most second-generation systems under standard sequencing conditions to approximately 35 to 400 bases. The array of DNA anchor locations can have a high density of DNA fragments, leading to extremely high overall throughput and a resultant low cost per identified base when the machine is run at high capacity. However, the disadvantages of second generation sequencing include short read length, variation in sequence equality with regard to representation bias and accuracy, complex sample preparation, the need for amplification, long time to result, the need for many samples to justify machine operation and significant data storage and interpretation requirements.

First and second generation sequencing technologies have led to a number of scientific advances. However, given the inherent limitations of these technologies, researchers still have not been able to unravel the complexity of genomes.

Pacific Biosciences’ Solution — Single Molecule, Real-Time Technology

We have developed our SMRT technology platform, which enables single molecule, real-time detection of biological processes. Based on our novel SMRT technology, we introduced the PacBio RS II System to address many of the limitations of the first and second generation technologies, by providing longer read lengths, elimination of amplification bias, increased flexibility, and reduced time to result. In addition, the PacBio RS II System, which includes the PacBio RS II instrument, consumables and software, enables the study of modified bases through its unique feature of detecting the kinetics of base incorporation during DNA synthesis.

Pacific Biosciences' SMRT Technology

SMRT technology enables the observation of DNA synthesis as it occurs in real time by harnessing the natural process of DNA replication, which in nature is a highly efficient and accurate process actuated by the DNA polymerase. The DNA polymerase attaches itself to a strand of DNA to be replicated, examines the individual base at the point it is attached, and then determines which of four building blocks, or nucleotides, is required to complement that individual base. After determining which nucleotide is required, the polymerase incorporates that nucleotide into the growing strand being produced. After incorporation, the enzyme advances to the next base to be replicated and the process is repeated.

To overcome the challenges inherent in real-time observation of the natural activity of the DNA polymerase, an enzyme 15 nanometers (nm) in diameter, we offer three key innovations:

- The SMRT Cell
- Phospholinked nucleotides
- The PacBio RS II instrument

The SMRT Cell

One of the fundamental challenges with observing a single DNA polymerase molecule working in real time is the ability to detect the incorporation of a single nucleotide, taken from a large pool of potential nucleotides, during DNA synthesis. To resolve this problem, we utilize our nanoscale innovation, the zero-mode waveguide, or ZMW.

A ZMW is a hole, tens of nanometers in diameter. The small size of the ZMW causes the intensity of visible laser light, which has a wavelength of approximately 600nm, to decay exponentially in the ZMW. Therefore, shining a laser up into the ZMW selectively illuminates only the bottom portion of the ZMW. DNA polymerases are anchored to the bottom of the glass surface of the ZMWs using a proprietary technique. Nucleotides, each type labeled with a different colored fluorophore, are then flooded above an array of ZMWs at the required concentration. When the labeled nucleotides diffuse into the bottom portion of the ZMWs, which contain the anchored DNA polymerases, their fluorescence can be monitored. When the correct nucleotide is detected by the polymerase, it is incorporated into the growing DNA strand in a process that takes milliseconds in contrast to simple diffusion which takes microseconds. This difference in time results in higher signal intensity for incorporated versus unincorporated nucleotides, which creates a high signal-to-noise ratio. Thus, the ZMW has the ability to detect a single incorporation event against the background of fluorescently labeled nucleotides at biologically relevant concentrations. Our DNA sequencing is performed on proprietary SMRT Cells, each having an array of approximately 150,000 ZMWs. Each ZMW is capable of containing a DNA polymerase molecule bound to a single DNA template. Currently, our immobilization process randomly distributes polymerases into ZMWs across the SMRT Cell, resulting in approximately one-third of the ZMWs having a single template.

Phospholinked Nucleotides

Our proprietary phospholinked nucleotides have a fluorescent dye attached to the phosphate chain of the nucleotide rather than to the base. As a natural step in the synthesis process, the phosphate chain is cleaved when the nucleotide is incorporated into the DNA strand. Thus, upon incorporation of a phospholinked nucleotide, the DNA polymerase naturally frees the dye molecule from the nucleotide when it cleaves the phosphate chain. Upon cleaving, the label quickly diffuses away, leaving a natural piece of DNA without evidence of labeling.

The PacBio RS II Instrument

The PacBio RS II instrument conducts, monitors, and analyzes single molecule biochemical reactions in real time. The instrument uses a high numerical aperture objective lens and four single-photon sensitive cameras to collect the light pulses emitted by fluorescent reagents allowing the observation of biological processes. An optimized set of algorithms is used to translate the information that is captured by the optics system. Using the recorded information, light pulses are converted into either an A, C, G or T base call with associated quality metrics. Once sequencing is started, the real-time data is delivered to the system's primary analysis pipeline, which outputs base identity and quality values, or QVs. To generate a consensus sequence from the data, an assembly process assembles the different fragments from each ZMW based on common sequences.

SMRT Sequencing Advantages

Sequencing based on our SMRT technology offers the following key benefits:

- Longer read lengths

SMRT technology has been demonstrated to produce read lengths that are significantly longer than those of first and second generation sequencing technologies. Long read lengths are necessary to span repetitive regions to efficiently assemble genomes. Long read lengths are an important factor in enabling a comprehensive view of the genome, as they can reveal multiple types of genetic variation such as structural variants.

- High consensus accuracy

3

Users of SMRT technology can achieve very high consensus accuracy due to the attributes of SMRT sequencing, including long read lengths, lack of amplification bias, and lower systematic bias. Users of second generation sequencing technologies often cannot achieve comparable results due to their shorter read lengths and systematic bias.

- More uniformity and less systematic error

The sample preparation step for SMRT sequencing does not require amplification; when amplification is not used during sample preparation, the reads are not subject to amplification bias. Importantly, this allows for uniform identification of all bases present in a DNA sample and uniform coverage. As a result, SMRT sequencing can detect and identify regions and entire genes that may be missed by second generation sequencing technologies.

- Ability to observe and capture kinetic information

The ability to observe the activity of a DNA polymerase in real time enables the PacBio RS II to collect, measure and assess the dynamics and timing of nucleotides being added to a growing DNA strand, referred to as kinetics. It is well established in the scientific community that chemical modification of DNA such as the addition of a methyl group, known as methylation, can alter the biological activity of the affected nucleotide. The PacBio RS II detects changes in kinetics automatically by capturing and recording changes in the duration of, and distances between, each of the fluorescent pulses during a typical sequencing analysis. Integrated software can then translate these kinetic signatures into uniquely characterized modified bases such as 6mA, 4mC and 5mC in bacteria. Other sequencing systems which rely on a sample preparation amplification step or limited by signal resolution are unable to directly measure this type of kinetic data.

- Flexibility

The PacBio RS II System has the ability to scale the throughput and cost of sequencing across a range of small to large projects. It can be used with a variety of sample types and can output a range of DNA lengths.

Our Products

We entered the market with our first commercial product, the PacBio RS and proprietary consumables, during the second quarter of 2011 and launched the higher performance PacBio RS II during the second quarter of 2013. The PacBio RS II System provides access to a wide range of applications. The system is designed for expandable capability to permit performance improvements and new applications to be delivered through chemistry and software enhancements without necessitating changes to the PacBio RS II instrument's hardware.

The PacBio RS II Instrument

The PacBio RS II instrument conducts, monitors, and analyzes biochemical sequencing reactions. The instrument is an integrated unit that includes high performance optics, automated liquid handling, a touchscreen control interface, a computational Blade Center and software. The instrument's high performance optics monitor thousands of ZMWs in real time. The automated liquid handling system performs reagent mixing and prepares SMRT Cells. The instrument's touchscreen control interface, the RS Touch, is the user's primary control center to design and monitor experiments. The Blade Center is the computational brain of the PacBio RS II instrument, responsible for processing

the sequencing data produced on the SMRT Cells. The PacBio RS II instrument has been designed to allow for performance improvements.

Consumables

Customers must purchase proprietary consumable products to run the PacBio RS II. Our consumable products include our proprietary SMRT Cells and reagent kits. One SMRT Cell is consumed per sequencing reaction on the PacBio RS II. Eight SMRT Cells are individually hermetically sealed and packaged together into a streamlined 8Pac format enabling researchers to choose the number of SMRT Cells they need per experiment.

We offer several reagent kits, each designed to address a specific step in the workflow. A template preparation kit is used to convert DNA into SMRTbell™ double-stranded DNA library formats and therefore includes typical molecular biology reagents, such as ligase, buffers and exonucleases. Our binding kits include our modified DNA polymerase, and are used to bind SMRTbell libraries to the polymerase in preparation for sequencing. Our sequencing kits contains reagents required for on-instrument, real-time sequencing, including the phospholinked nucleotides.

Product Enhancements

During 2014, we continued to significantly enhance the performance of the PacBio RS II System through a combination of sample preparation protocol enhancements, software releases, and the release of a new sequencing reagent chemistry. By providing an increasing number of longer reads per instrument run, the new chemistry enables users to assemble more genomes to a high quality. We have continually improved our software to expand the number of supported applications such as large genome assembly, sequencing of transcript isoforms produced from genes, and phasing of haplotypes in large amplicons. During 2015 we plan to further

improve our existing products, including chemistry and sample preparation improvements to increase throughput and expand our supported applications, and to develop new products.

Market for Our Products

Our customers use our products for sequencing genomes and transcriptomes across a wide range of organisms. Initially customers in research, government and commercial markets used the PacBio RS II to generate more complete assemblies of small and medium size genomes, such as bacteria and fungi, and for sequencing targeted regions of larger genomes such as humans and plants. As throughput and read lengths have increased, the complexity and size of genomes being resolved with SMRT sequencing has grown. Scientists now use SMRT sequencing to generate genome assemblies of humans, plants & animals, characterize transcriptomes through full-length isoform sequencing, and phase complex genomic regions like full-length HLA genes. We plan to continue increasing throughput and read lengths with future product enhancements, and to seek increased sales of our products in research and commercial markets such as human biomedical research, agriculture & biotechnology, microbiology & infectious disease, and immunogenomics.

There are a number of emerging markets for sequencing-based tests, including molecular diagnostics, which represent significant potential opportunities for our products. The development of these markets is subject to variability driven by ongoing changes in the competitive landscape, evolving regulatory requirements, government funding of research and development activities, and macroeconomic conditions. Introductions of new technologies and products, while positive to the overall development of these markets, may result in greater competition for the limited financial resources available. As we continue to expand into these emerging markets, the development of our business will be impacted by the variability of the factors affecting the growth of these markets.

Pacific Biosciences' Strategy

We plan to execute the following strategy:

- Offer differentiated products based on our proprietary SMRT technology

Our SMRT technology provides a window into biological processes that has not previously been available. The combination of our products' and underlying SMRT technology's ability to deliver long read lengths, high consensus accuracy, low bias, and kinetic information afford the scientific community a new tool to conduct research not possible with first and second generation sequencing instruments.

- Enhance product performance and introduce new products to increase market share.

The design of the PacBio RS II allows for significant performance improvements. Our flexible platform is designed to generate a recurring revenue stream through the sale of proprietary SMRT Cells and reagent kits. We plan to introduce additional product enhancements to further reduce DNA sequencing project cost and time to result while expanding application solutions. During 2014, we introduced a new sequencing chemistry, a variety of sample preparation improvements, and made significant enhancements to our software analysis toolkit. In addition, the software analysis tools have improved the ease of use of our products and have enabled our customers to take greater advantage of their SMRT sequencing data. We plan to continue introducing enhancements to our products over time and to develop new products.

- Leverage SMRT technology and community engagement to expand application capabilities and penetrate new markets.

We plan to leverage our customers' successes with our SMRT technology platform to expand its capabilities in applications our customers have identified as high-value because SMRT sequencing offers differentiated capabilities. Early applications identified by our customers include: de novo genome assembly, targeted sequencing of complex regions, isoform characterization, and epigenetic analysis. We plan to develop whole product solutions around these applications, making it easier for customers who are not typically early adopters of new technology to take advantage of SMRT sequencing.

In 2013, we entered into a collaboration agreement with Roche to jointly develop products based on our SMRT technology for the human in vitro diagnostics market. In the long term, we believe that our SMRT technology may also be adapted for RNA transcription monitoring, direct RNA sequencing, protein translation and ligand binding. We believe these applications can create substantial new markets for our technology.

- Create a global community of users to enhance informatics capabilities, develop sample preparation solutions, and drive adoption of our products in new application and market areas.

We work closely with our customers and collaborators to develop new applications and demonstrate SMRT sequencing capabilities on scientifically relevant projects. We partner with members of the informatics community to develop and define standards for working with single molecule, real-time sequence data. We maintain the PacBio DevNet site, a website on which we make available various software tools and information about our SMRT sequencing technology to support academic informatics developers, life scientists and independent software vendors interested in creating tools to work with SMRT sequencing data. This gives the user flexibility to perform further analysis of the sequencing data through third-party

software or share data with collaborators. To maximize the flexibility and functionality for all users, all of our secondary analysis algorithms are made available under an open source license. We also maintain the PacBio SampleNet site, a website on which we make available various methods developed internally and externally for simplifying and enhancing sample preparation protocols.

Marketing, Sales, Service and Support

We market our products through a direct sales force in North America and Europe and primarily through distributors in Asia. Our sales strategy involves the use of a combination of sales personnel and field application scientists. The role of our sales personnel is to educate customers on the advantages of SMRT technology and the applications that our technology makes possible. The role of our field application scientists is to provide on-site training and scientific technical support to prospective and existing customers. Our field application scientists are technical experts, often with advanced degrees, and generally have extensive experience in academic research and core sequencing lab experience.

Service for our instruments is performed by field service engineers. These field service engineers are trained by experienced personnel to test, trouble-shoot, and service instruments installed at customer sites.

In addition, we maintain an applications lab team in Menlo Park, California composed of scientific experts who can transfer knowledge from the research and development team to the field application scientists. The applications lab team also runs foundational scientific collaborations and proof of principle studies, which help demonstrate the value of our product offering to prospective customers.

Customers

Our customers include research institutions, commercial laboratories, genome centers, clinical, government and academic institutions, genomics service providers, pharmaceutical companies and agricultural companies. In general, our customers will isolate, prepare and analyze genetic samples using the PacBio RS II System in their own research labs to address their specific applications and scientific questions. For example, customers in academic research institutions may have bacteria, animal, or human DNA samples isolated from various sources while agricultural biology companies may have DNA samples isolated from different strains of rice, corn or other crops. For year ended December 31, 2014, contractual revenue from Roche accounted for more than 10% of our total revenue. For each of the years ended December 31, 2013 and 2012, no single end customer accounted for more than 10% of our total revenue.

We believe that the majority of our current customers are early adopters of sequencing technology. By focusing our efforts on high-value applications, and developing whole product solutions around these applications, we seek to drive the adoption of our products across a broader customer base and into numerous large-scale projects. In general, the broader adoption of new technologies by mainstream customers can take a number of years.

We currently sell our products to a number of customers outside the United States, including customers in other areas of North America, Europe, and Asia. Revenue from customers outside the United States totaled \$26.2 million, or 43% of our total revenue, during fiscal 2014, compared to \$14.6 million, or 52% of our total revenue, during fiscal 2013, compared to \$14.6 million, or 56%, in fiscal 2012.

Backlog

As of December 31, 2014, our instrument backlog was approximately \$8.4 million, compared to \$7.4 million at December 31, 2013. We define backlog as purchase orders or signed contracts from our customers which we believe are firm and for which we have not yet recognized revenue. We expect to convert this backlog to revenue during 2015 subject to customers who may otherwise seek to cancel or delay their orders even if we are prepared to fulfill them.

Manufacturing

Our principal manufacturing facilities are located at our headquarters in Menlo Park, California. We currently perform some of the manufacturing and all of the final integration of our instruments in-house, while outsourcing most sub-assemblies to third-party manufacturers. With respect to the manufacture of SMRT Cells, we subcontract wafer fabrication and processing to semiconductor processing facilities, but conduct critical surface treatment processes internally. In addition, we currently manufacture critical reagents in-house, including our phospholinked nucleotides and our DNA polymerase.

We purchase both custom and off-the-shelf components from a large number of suppliers and subject them to significant quality specifications. We periodically conduct quality audits of most critical suppliers and have established a supplier certification program. We purchase components through purchase orders. Some of the components required in our products are currently either sole sourced or single sourced.

Research and Development

Our SMRT technology requires the blending of a number of unique disciplines, namely nanofabrication, physics, photonics, optics, molecular biology, engineering, signal processing, high performance computing, and bioinformatics. Our research and

development team is a blend of these disciplines creating a single, cross-functional operational unit. We have also established productive working relationships with technology industry leaders, as well as leading academic centers, to augment and complement our internal research and development efforts. Research and development expense incurred was \$48.2 million, \$45.2 million and \$47.6 million during 2014, 2013 and 2012, respectively. We plan to continue investment in research and development to enhance the performance and expand the application of our current products, and introduce additional products based on our SMRT technology. Our goals include further improvements in sequencing read length and mappable data per SMRT Cell, chemistry and software enhancements for expanding base modification analysis, and enhancements in sample preparation and bioinformatics tools that take advantage of the capabilities of our products. In addition, our engineering teams will continue their focus on increasing instrument component and system reliability, reducing costs, and implementing additional system flexibility and versatility through the enhancement of existing products and development of new products.

Intellectual Property

Developing and maintaining a strong intellectual property position is an important element of our business. We have sought patent protection for our SMRT technology, and may seek patent protection for improvements and ancillary technology conceived in developing our SMRT technology if we believe such protection will be advantageous.

Our current patent portfolio, including patents exclusively licensed to us, is directed to various technologies, including SMRT nucleic acid sequencing and other methods for analyzing biological samples, ZMW arrays, surface treatments for such ZMW arrays, phospholinked nucleotides and other reagents for use in nucleic acid sequencing, optical components and systems, processes for identifying nucleotides within nucleic acid sequences and processes for analysis and comparison of nucleic acid sequence data. Some of the patents and applications that we own, as well as some of the patents and applications that we have licensed from other parties, are subject to U.S. government march-in rights, whereby the U.S. government may disregard our exclusive patent rights on its own behalf or on behalf of third parties by imposing licenses in certain circumstances, such as if we fail to achieve practical application of the U.S. government funded technology, because action is necessary to alleviate health or safety needs, to meet requirements of federal regulations, or to give preference to U.S. industry. In addition, U.S. government funded inventions must be reported to the government and U.S. government funding must be disclosed in any resulting patent applications.

As of December 31, 2014, we own or hold exclusive licenses to 163 issued U.S. patents, 108 pending U.S. patent applications, 66 granted foreign patents and 99 pending foreign patent applications, including foreign counterparts of U.S. patent and patent applications. The full term of the issued U.S. patents will expire between 2016 and 2033. We also have non-exclusive patent licenses with various third parties to supplement our own large and robust patent portfolio.

Of these patents and patent applications, 22 issued U.S. patents, one pending U.S. patent application, 14 granted foreign patents and one pending foreign patent application are licensed to us by the Cornell Research Foundation, which manages technology transfers on behalf of Cornell University, collectively referred to as Cornell. We have also entered into a license agreement with Indiana University Research and Technology Corporation, or IURTC, for U.S. Patent No. 6,399,335, which relates to nucleoside triphosphates that include a labeling group attached through the terminal phosphate group in the triphosphate chain. We have also entered into a license agreement with GE Healthcare Bio-Sciences Corp, or GE Healthcare, for several U.S. and foreign patents and pending patent applications related to labeled nucleoside polyphosphate compounds.

In September 2013, we entered into a Development, Commercialization and License Agreement (the "Roche Agreement") with Roche, pursuant to which we: (i) will develop diagnostic products for clinical use including sequencing systems and consumables based on our proprietary SMRT technology; (ii) granted to Roche an exclusive right to commercialize, and an exclusive license to sell, the developed diagnostic products for clinical use; and (iii)

will manufacture and supply certain products intended for clinical use as the exclusive supplier to Roche. We received a non-refundable up-front payment of \$35.0 million in 2013 and a milestone payment of \$10.0 million in 2014 pursuant to the Roche Agreement. Under the terms of the Roche Agreement, we may receive up to an additional \$30.0 million based on the achievement of additional development milestones in future periods. The Roche Agreement has an initial term of thirteen years and provisions allowing Roche five-year renewals.

Where patent protection is difficult to obtain or difficult to enforce for a particular technological development or the technological development derives greater value from being maintained as confidential information, we seek to protect such information as a trade secret.

Competition

Given the market opportunity, there are a significant number of competing companies offering DNA sequencing equipment or consumables. These include Illumina, Inc. and Thermo Fisher Scientific Inc. These companies currently have greater financial, technical, research and/or other resources than we do. They also have larger and more established manufacturing capabilities and marketing, sales and support functions. We expect the competition to intensify within this market as there are also several companies in the process of developing new technologies, products and services. Increased competition may result in pricing pressures, which could harm our sales, profitability or market share.

In order for us to successfully compete against these companies, we will need to demonstrate that our products deliver superior performance and value as a result of our key differentiators, including single molecule, real-time resolution, long read length, fast time to result and flexibility, as well as the breadth and depth of current and future products and applications.

Employees

As of December 31, 2014, we had 344 full-time employees. Of these employees, 134 were in research and development, 62 were in operations, 101 were in marketing, sales, service and support, and 47 were in general and administration. With the exception of our field-based sales and service teams, substantially all of our employees are located at our headquarters in Menlo Park, California. None of our employees are represented by labor unions or are covered by a collective bargaining agreement with respect to their employment. We have not experienced any work stoppages, and we consider our relationship with our employees to be good.

Available Information

Our website is located at www.pacb.com. The information posted on our website is not incorporated into this Annual Report on Form 10-K. Our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and amendments to reports filed or furnished pursuant to Sections 13(a) and 15(d) of the Securities Exchange Act of 1934, as amended, are available free of charge through the “Investors” section of our website as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC.

Additionally, we use our website as a channel of distribution for important company information. Important information, including press releases, analyst presentations and financial information regarding us, as well as corporate governance information, is routinely posted and accessible on the “Investor Relations” section of the website, which is accessible by clicking on the tab labeled “About Us - Investors” on our website home page. In addition, important information is routinely posted and accessible on the blog section of our website, which is accessible by clicking on the tab labeled “Blog” on our website home page, as well as our Twitter account (@pacbio). Information on or that can be accessed through our website or our Twitter account is not part of this Annual Report on Form 10-K, and the inclusion of our website address is an inactive textual reference only.

ITEM 1A. RISK FACTORS

You should consider carefully the risks and uncertainties described below, together with all of the other information in this Annual Report on Form 10-K, which could materially affect our business, financial condition, results of operations and prospects. The risks described below are not the only risks facing us. Risks and uncertainties not currently known to us or that we currently deem to be immaterial also may materially affect our business, financial condition, results of operations and prospects.

Risks Related to Our Business

We have limited experience as a commercial company.

Our first commercial product launched in 2011 and we have limited sales to date and as such, we have limited historical financial data upon which to base our projected revenue, planned operating expense or upon which to evaluate us and our commercial prospects. Based on our limited experience in developing and marketing new products, we may not be able to effectively:

- drive adoption of our current and future products;
- attract and retain customers for our products;
- provide appropriate levels of customer training and support for our products;
- implement an effective marketing strategy to promote awareness of our products;
- develop and commercialize new products or achieve an acceptable return, on our research and development efforts and expenses;
- comply with regulatory requirements applicable to our products;
- anticipate and adapt to changes in our market;
- maintain and develop strategic relationships with vendors and manufacturers to acquire necessary materials for the production of our existing or future products;
- scale our manufacturing activities to meet potential demand at a reasonable cost;
- avoid infringement and misappropriation of third-party intellectual property;
- obtain licenses to third-party intellectual property on commercially reasonable terms;
- obtain valid and enforceable patents that give us a competitive advantage;
- protect our proprietary technology; and

- attract, retain and motivate qualified personnel.

In addition, a high percentage of our expenses is and will continue to be fixed. Accordingly, if we do not generate revenue as and when anticipated, our losses may be greater than expected and our operating results will suffer.

We have incurred losses to date, and we expect to continue to incur significant losses as we develop our business and may never achieve profitability.

We have incurred net losses since inception and we cannot be certain if or when we will produce sufficient revenue from our operations to support our costs. Even if profitability is achieved, we may not be able to sustain profitability. We expect to continue to incur substantial losses and negative cash flow from operations for the foreseeable future.

If our products fail to achieve and sustain sufficient market acceptance, we will not generate expected revenue and our business may not succeed.

We cannot be sure that our current or future products will gain acceptance in the marketplace at levels sufficient to support our costs. Our success depends, in part, on our ability to expand the market for genetic analysis to include new applications that are not practicable with other current technologies. To accomplish this, we must successfully commercialize, and continue development of, our proprietary Single Molecule, Real-Time (SMRT) technology for use in a variety of life science and other applications. There can be no assurance that we will be successful in securing additional customers for our products. Furthermore, we cannot guarantee that our products will be satisfactory to potential customers in the markets we seek to reach. These markets are dynamic, and there can be no assurance that they will develop as quickly as we expect or that they will reach their full potential. As a result, we may be required to refocus our marketing efforts, and we may have to make changes to the specifications of our products to enhance our ability to enter particular markets more quickly. Even if we are able to implement our technology successfully, we and/or our sales and distribution partners may fail to achieve or sustain market acceptance of our current or future products by academic, government and clinical laboratories and pharmaceutical, diagnostic, biotechnology and agriculture companies, among others, across the full range of our

intended life science and other applications. If the market for our products grows more slowly than anticipated, if competitors develop better or more cost-effective products or if we are unable to further grow our customer base, our future sales and revenue would be materially harmed and our business may not succeed.

Our development and commercialization of future products, including those related to our arrangement with Roche, may not result in the benefits we anticipate, and could have a material adverse effect on our business, financial condition and results of operations.

We entered into an agreement with F. Hoffman-La Roche Ltd. (“Roche”), pursuant to which we are developing and expect to manufacture diagnostic products for clinical use, including sequencing systems and consumables based on our proprietary SMRT technology (the “Roche Agreement”), and we are engaged in research and development efforts, which, if successful, may result in the introduction of new products in the future. Our research and development efforts are complex and require us to incur substantial expenses. We may not be able to develop and commercialize new products or achieve an acceptable return, if any, on our research and development efforts and expenses. There can also be no assurance that we will be able to develop and manufacture future products as provided by the terms of the Roche Agreement or that Roche will be able to commercialize and sell the developed diagnostic products. We may also be unable to meet the additional development milestones required for additional payments from Roche. We could also be involved in disputes with Roche, which could lead to delays in or termination of our development and manufacture of diagnostic products and result in time-consuming and expensive litigation or arbitration. In addition, any such dispute could diminish Roche’s commitment to us and reduce the resources they devote to commercializing the developed diagnostic products. If Roche terminates or breaches the Roche Agreement, or otherwise acquires, develops and/or commercializes alternative or competing products, the successful commercialization of our diagnostic products for clinical use would be materially and adversely affected.

If we are not able to realize the benefits we anticipate from the development and commercialization of future products, including the expected benefits from the Roche Agreement, it could have a material adverse effect on our business, financial condition and results of operations. In addition, the introduction of future products may lead to our limiting or ceasing development of further enhancements to our existing products, as we focus our resources on the new products, and could result in reduced marketplace acceptance and loss of sales of our existing products, materially adversely affecting our revenue and operating results. New products may also have quality or other defects, especially in the early stages of introduction. If we do not successfully manage product transitions, our business, reputation and financial condition may be materially adversely harmed.

Rapidly changing technology in life sciences and diagnostics could make the products we are developing obsolete unless we continue to develop and commercialize new and improved products and pursue new market opportunities.

Our industry is characterized by rapid and significant technological changes, frequent new product introductions and enhancements and evolving industry standards. Our future success will depend on our ability to continually improve our products, to develop and introduce new products that address the evolving needs of our customers on a timely and cost-effective basis and to pursue new market opportunities. These new market opportunities may be outside the scope of our proven expertise or in areas where the market demand is unproven, and new products and services developed by us may not gain market acceptance. Our inability to develop and introduce new products and to gain market acceptance of new products could harm our future operating results. Unanticipated difficulties or delays in replacing existing products with new products or in commercializing improved or new products in sufficient quantities to meet customer demand could diminish future demand for our products and harm our future operating results.

Increased market adoption of our products by customers may depend on the availability of sample preparation and informatics tools, some of which may be developed by third parties.

Our commercial success may depend in part upon the development of sample preparation and software and informatics tools by third parties for use with our products. We cannot guarantee that third parties will develop tools that our customers or potential customers will find useful with our products. A lack of additional available complementary sample preparation and informatics tools may impede the adoption of our products and may adversely impact our business.

We operate in a highly competitive industry and if we are not able to compete effectively, our business and operating results will likely be harmed.

Some of our current competitors, including Illumina, Inc. and Thermo Fisher Scientific Inc., as well as other potential competitors, have greater name recognition, more substantial intellectual property portfolios, longer operating histories, significantly greater financial, technical, research and/or other resources, more substantial experience in new product development, larger and more established manufacturing capabilities and marketing, sales and support functions, and/or more established distribution channels to deliver products to customers than we do. These competitors may be able to respond more quickly and effectively than we can to new or changing opportunities, technologies, standards or customer requirements. In light of these advantages, even if our technology is more effective than the products or service offerings of our competitors, current or potential customers might purchase competitive products and services instead of our products. Increased competition may result in pricing pressures, which could harm our sales, profitability or market share. Our failure to further enhance our existing products and to introduce new products to compete effectively could materially and adversely affect our business, financial condition or results of operations.

We may be unable to successfully increase sales of our products.

Our ability to achieve profitability depends on our ability to attract customers for our current and future products, and we may be unable to effectively market our products. To perform sales, marketing, distribution and customer support functions successfully, we face a number of risks, including:

- our ability to attract, retain and manage the sales, marketing and service personnel necessary to expand market acceptance for our technologies;
- the time and cost of maintaining and growing a specialized sales, marketing and service force for a particular application, which may be difficult to justify in light of the revenue generated; and
- our sales, marketing and service force may be unable to execute successful commercial activities.

We have enlisted and may continue to enlist third parties to assist with sales, distribution and customer support. There is no guarantee that we will be successful in attracting desirable sales and distribution partners or that we will be able to enter into arrangements with such partners on terms favorable to us. If our sales and marketing efforts, or those of any of our third-party sales and distribution partners, are not successful, our technologies and products may not gain market acceptance, which could materially impact our business operations.

We rely on other companies for the manufacture of certain components and sub-assemblies and intend to outsource additional sub-assemblies in the future. We may not be able to successfully scale the manufacturing process necessary to build and test multiple products on a full commercial basis, which could materially harm our business.

Our products are complex and involve a large number of unique components, many of which require precision manufacturing. The nature of the products requires customized components that are currently available only from a limited number of sources, and in some cases, single sources. We have chosen to source certain critical components from a single source, including suppliers for our SMRT Cells, reagents and instruments. If we are required to purchase these components from an alternative source, it could take several months or longer to qualify the alternative sources. If we are unable to secure a sufficient supply of these product components on a timely basis, our operations and manufacturing will be adversely affected, we could be unable to meet customer demand and our business and results of operations may be adversely affected.

The operations of our third-party manufacturing partners and suppliers could be disrupted by conditions unrelated to our business or operations or that are beyond our control. If our manufacturing partners or suppliers are unable or fail to fulfill their obligations to us for any reason, we may not be able to manufacture our products and satisfy customer demand or our obligations under sales agreements in a timely manner, and our business could be harmed as a result. Our current manufacturing process is characterized by long lead times between the ordering and delivery of our products. If we have ordered insufficient components to manufacture our products on a timely basis to meet customer demand, our sales and our gross margin may be adversely affected and our business could be materially harmed. If we are unable to reduce our manufacturing costs and establish and maintain reliable high volume manufacturing suppliers as we scale our operations, our business could be materially harmed.

We may be unable to consistently manufacture our instruments and consumable kits, including SMRT Cells, to the specifications required by our customers or in quantities necessary to meet demand at an acceptable cost.

In order to successfully derive revenue from our products, we need to supply our customers with products that meet their specifications, quality requirements and expectations. Our customers have previously experienced variability in the performance of our instruments and SMRT Cells. There is no assurance that we will be able to manufacture our

products so that they consistently achieve the product specifications and quality that our customers expect, including those products and specifications that may be developed pursuant to the Roche Agreement. There is also no assurance that we will be able to increase manufacturing yields and decrease costs, or that we will be successful in forecasting customer demand or manufacturing and supply costs. Furthermore, we may not be able to increase manufacturing to meet anticipated demand. An inability to manufacture products that consistently meet specifications, in necessary quantities and at commercially acceptable costs, will have a negative material impact on our business.

We intend to raise additional financing to fund our existing operations. Equity and debt securities we issue may have rights senior to common stockholders.

We intend to raise additional funds through public or private debt or equity financing. Additional funds may not be available on terms acceptable to us or at all, particularly in light of restrictions under our debt agreement. We have incurred and may further incur additional debt. Debt holders have rights senior to common stockholders to make claims on our assets and the terms of our existing debt agreement restrict certain activities, including our ability to pay dividends on our common stock.

Our indebtedness could adversely affect our financial condition and prevent us from fulfilling our obligations.

Our net losses since inception and our expectation of incurring substantial losses and negative cash flow for the foreseeable future, combined with our existing indebtedness, could:

- make it more difficult for us to satisfy our obligations, including under the debt agreement;

- increase our vulnerability to general adverse economic and industry conditions;
- limit our ability to fund future working capital, capital expenditures, research and development and other business opportunities;
- require us to dedicate a substantial portion of our cash flow from operations to service payments on our indebtedness;
- increase the volatility of the price of our common stock;
- limit our flexibility to react to changes in our business and the industry in which we operate;
- place us at a competitive disadvantage to our competitors that have less or no indebtedness; and
- limit, along with the financial and other restrictive covenants in our indebtedness, among other things, our ability to borrow additional funds.

Our existing debt contains covenants which may adversely impact our business and our failure to comply with such covenants could cause our outstanding indebtedness to become immediately payable.

Our existing debt contains various affirmative and negative covenants, including restrictions on our and our subsidiaries' ability to incur additional indebtedness or liens on our assets. These covenants impose significant operating and financial restrictions on us, including restrictions on our ability to take certain actions that may be in our best interests.

A breach of any of the covenants contained in our debt could result in an event of default. If an event of default exists, debt holders could elect to declare all amounts outstanding under the debt to be immediately due and payable. If we are unable to repay our indebtedness when due and payable, debt holders could proceed against the collateral granted to them to secure such indebtedness. We have pledged substantially all of our property and interests in property, including our intellectual property, as collateral under our existing debt. If the debt holders accelerate the repayment of our indebtedness, we may not have sufficient funds to make such repayment, which could have a material adverse effect on our liquidity and ability to conduct our business.

In addition, at the election of the holders representing a majority of the aggregate principal amount of the outstanding notes issued pursuant to our existing debt agreement, the holders may elect to receive 25% of the net proceeds from any financing that includes an equity component, including without limitation, the sale or issuance of our common stock, options, warrants or other securities convertible or exchangeable for shares of our common stock, as payment of the notes. This right is subject to certain exceptions set forth in our existing debt agreement, including that the right will not apply until we have issued 15.0 million shares of our common stock following the date of our existing debt agreement. To the extent we raise additional capital in the future through the sale of common stock under our "at the market" offering or through other financing activities, we may be obligated, at the election of the holders of the notes, to pay 25% of the net proceeds from any such financing activities as payment of the notes.

Our products are highly complex and have recurring support requirements.

In light of the highly complex technology involved in our products, there can be no assurance that we will be able to continue providing adequate support for our products. Our customers have in the past experienced reliability issues with our products. If our products have reliability or other quality issues or require unexpected levels of support in the future, the market acceptance and utilization of our products may not grow to levels sufficient to support our costs and our reputation and business could be harmed. We generally deliver our sequencing instruments with one year of service included in the purchase price and offer additional years of service for an additional fee. If our service and support costs increase, our business and operations may be adversely affected.

Our products could have unknown defects or errors, which may give rise to claims against us or divert application of our resources from other purposes.

Products using our SMRT technology are complex and may develop or contain undetected defects or errors. We cannot provide assurance that material performance problems will not arise. Despite testing, defects or errors may arise in our products, which could result in a failure to achieve increased market acceptance, diversion of development resources, injury to our reputation and increased warranty, service and maintenance costs. We generally ship our sequencing instruments with one year of service included in the purchase price with an option to purchase one or more additional years of service. We also provide a warranty for our consumables, which is generally limited to replacing, or at our option, giving credit for, any consumable with defects in material or workmanship. Defects or errors in our products may also discourage customers from purchasing our products. The costs incurred in correcting any defects or errors may be substantial and could adversely affect our operating margins. In addition, such defects or errors could lead to the filing of product liability claims against us or against third parties who we may have an obligation to indemnify against such claims, which could be costly and time-consuming to defend and result in substantial damages. Although we have product liability insurance, any product liability insurance that we have or procure in the future may not protect our business from the financial impact of a product liability claim. Moreover, we may not be able to obtain adequate insurance coverage on acceptable terms. Any insurance that we have or obtain will be subject to deductibles and coverage limits. A product liability claim could have a serious adverse effect on our business, financial condition and results of operations.

We depend on the continuing efforts of our senior management team and other key personnel. If we lose members of our senior management team or other key personnel or are unable to successfully retain, recruit and train qualified scientists, engineering and other personnel, our ability to develop our products could be harmed, and we may be unable to achieve our goals.

Our future success depends upon the continuing services of members of our senior management team and scientific and engineering personnel. In particular, our scientists and engineers are critical to our future technological and product innovations and we will need to hire additional qualified personnel. Our industry, particularly in the San Francisco Bay Area, is characterized by high demand and intense competition for talent, and the turnover rate can be high. We compete for qualified management and scientific personnel with other life science companies, academic institutions and research institutions, particularly those focusing on genomics. Our employees could leave our company with little or no prior notice and would be free to work for a competitor. If one or more of our senior executives or other key personnel were unable or unwilling to continue in their present positions, we may not be able to replace them easily or at all, and other senior management may be required to divert attention from other aspects of the business. In addition, we do not have “key person” life insurance policies covering any member of our management team or other key personnel. The loss of any of these individuals or any inability to attract or retain qualified personnel, including scientists, engineers and others, could prevent us from pursuing collaborations and adversely affect our product development and introductions, business growth prospects, results of operations and financial condition.

A significant portion of our potential sales depends on customers’ spending budgets that may be subject to significant and unexpected variation which could have a negative effect on the demand for our products.

Our instrument sales represent significant capital purchases for our customers. Potential customers for our current or future products include academic and government institutions, genome centers, medical research institutions, clinical laboratories, pharmaceutical, agricultural, biotechnology, diagnostic and chemical companies. Their spending budgets can have a significant effect on the demand for our products. Spending budgets are based on a wide variety of factors, including the allocation of available resources to make purchases, funding from government sources which is highly uncertain, the spending priorities among various types of research equipment and policies regarding capital expenditures during economically uncertain periods. Any decrease in capital spending or change in spending priorities of our customers and potential customers could significantly reduce the demand for our products. Any delay or reduction in purchases by potential customers or our inability to forecast fluctuations in demand could harm our future operating results.

We may not be able to convert our orders in backlog into revenue.

Our backlog represents product orders from our customers that we have confirmed and for which we have not yet recognized revenue. We may not receive revenue from these orders, and the order backlog we report may not be indicative of our future revenue.

Many events can cause an order to be delayed or not completed at all, some of which may be out of our control. If we delay fulfilling customer orders, those customers may seek to cancel their orders with us. In addition, customers may otherwise seek to cancel or delay their orders even if we are prepared to fulfill them. If our orders in backlog do not result in sales, our operating results may suffer.

Delivery of our products could be delayed or disrupted by factors beyond our control, and we could lose customers as a result.

We rely on third-party carriers for the timely delivery of our products. As a result, we are subject to carrier disruptions and increased costs that are beyond our control. Any failure to deliver products to our customers in a safe and timely manner may damage our reputation and brand and could cause us to lose customers. If our relationship with any of these third-party carriers is terminated or impaired or if any of these third parties are unable to deliver our products, the delivery and acceptance of our products by our customers may be delayed, which could harm our business and financial results. The failure to deliver our products in a safe and timely manner may harm our relationship with our customers, increase our costs and otherwise disrupt our operations.

We are, and may become, subject to governmental regulations that may impose burdens on our operations, and the markets for our products may be narrowed.

We are subject, both directly and indirectly, to the adverse impact of government regulation of our operations and markets. For example, export of our instruments may be subject to strict regulatory control in a number of jurisdictions. The failure to satisfy export control criteria or to obtain necessary clearances could delay or prevent shipment of products, which could adversely affect our revenue and profitability. Moreover, the life sciences industry, which is expected to be one of the primary markets for our technology, has historically been heavily regulated. There are, for example, laws in several jurisdictions restricting research in genetic engineering, which may narrow our markets. Given the evolving nature of this industry, legislative bodies or regulatory authorities may adopt additional regulations that may adversely affect our market opportunities. Additionally, if ethical and other concerns surrounding the use of genetic information, diagnostics or therapies become widespread, there may be less demand for our products. Our business is also directly affected by a wide variety of government regulations applicable to business enterprises generally and to companies operating in the life science industry in particular. Failure to comply with government regulations or obtain or maintain necessary permits and licenses could result in a variety of fines or other censures or an interruption in our business operations which may have a negative impact on our ability to generate revenue and could increase the cost of operating our business

Our products could in the future be subject to regulation by the U.S. Food and Drug Administration or other domestic and international regulatory agencies, which could increase our costs and delay our commercialization efforts, thereby materially and adversely affecting our business and results of operations.

Our products are not currently subject to U.S. Food and Drug Administration, or FDA, clearance or approval since they are not intended for use in the diagnosis or treatment of disease. However, in the future, certain of our products or related applications could be subject to FDA regulation, or the FDA's regulatory jurisdiction could be expanded to include our products. Even where a product is exempted from FDA clearance or approval, the FDA may impose restrictions as to the types of customers to which we or our partners can market and sell our products. Such regulation and restrictions may materially and adversely affect our business, financial condition and results of operations.

Many countries have laws and regulations that could affect our products. The number and scope of these requirements are increasing. Unlike many of our competitors, this is an area where we do not have expertise. We, or our other third-party sales and distribution partners, may not be able to obtain regulatory approvals in such countries or may incur significant costs in obtaining or maintaining our foreign regulatory approvals. In addition, the export by us of certain of our products, which have not yet been cleared for domestic commercial distribution, may be subject to FDA or other export restrictions.

Doing business internationally creates operational and financial risks for our business.

Conducting and launching operations on an international scale requires close coordination of activities across multiple jurisdictions and time zones and consumes significant management resources. If we fail to coordinate and manage these activities effectively, our business, financial condition or results of operations could be adversely affected. International operations entail a variety of risks, including challenges in staffing and managing foreign operations, tariffs and other trade barriers, unexpected changes in legislative or regulatory requirements of foreign countries into which we sell our products, difficulties in obtaining export licenses or in overcoming other trade barriers and restrictions resulting in delivery delays and significant taxes or other burdens of complying with a variety of foreign laws. In conducting our international operations, we will be subject to U.S. laws relating to our international activities, as well as foreign laws relating to our activities in other countries. Failure to comply with these laws may subject us to financial and other penalties in the U.S. and foreign countries that could impact our operations or financial condition.

Changes in the value of the relevant currencies may affect the cost of certain items required in our operations. Changes in currency exchange rates may also affect the relative prices at which we are able to sell products in the same market. Our revenue from international customers may be negatively impacted as increases in the U.S. dollar relative to our international customers' local currencies could make our products more expensive, impacting our ability to compete. Our costs of materials from international suppliers may increase as the value of the U.S. dollar decreases relative to their local currency. Foreign policies and actions regarding currency valuation could result in actions by the United States and other countries to offset the effects of such fluctuations. Such actions may adversely impact our financial condition and results of operations.

If we fail to maintain proper and effective internal controls, our ability to produce accurate financial statements on a timely basis could be impaired, which would adversely affect our business and our stock price.

Ensuring that we have adequate internal financial and accounting controls and procedures in place to produce accurate financial statements on a timely basis is a costly and time-consuming effort that needs to be re-evaluated frequently. We may in the future discover areas of our internal financial and accounting controls and procedures that need improvement. Operating as a public company requires sufficient resources within the accounting and finance functions in order to produce timely financial information, ensure the level of segregation of duties, and maintain adequate internal control over financial reporting customary for a U.S. public company.

Our management is responsible for establishing and maintaining adequate internal control over financial reporting to provide reasonable assurance regarding the reliability of our financial reporting and the preparation of financial statements for external purposes in accordance with U.S. generally accepted accounting principles. Our management does not expect that our internal control over financial reporting will prevent or detect all errors and all fraud. A control system, no matter how well designed and operated, can provide only reasonable, not absolute, assurance that the control system's objectives will be met. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that misstatements due to error or fraud will not occur or that all control issues and instances of fraud, if any, within our company will have been detected.

Pursuant to Section 404 of the Sarbanes-Oxley Act, we perform periodic evaluations of our internal control over financial reporting. While we have in the past performed this evaluation and concluded that our internal control over financial reporting was operating effectively, there can be no assurance that in the future material weaknesses or significant deficiencies will not exist or otherwise be discovered. In addition, if we are unable to produce accurate financial statements on a timely basis, investors could lose confidence in the reliability of our financial statements, which could cause the market price of our common stock to decline and make it more difficult for us to finance our operations and growth.

Our ability to use net operating losses to offset future taxable income may be subject to substantial limitations.

Under Section 382 of the Internal Revenue Code, a corporation that undergoes an "ownership change" is subject to limitations on its ability to utilize its pre-change net operating losses, or NOLs, to offset future taxable income. We believe that we have had one

or more ownership changes, as a result of which our existing NOLs are currently subject to limitation. Future changes in our stock ownership could result in additional ownership changes under Section 382. We may not be able to utilize a material portion of our NOLs, even if we attain profitability.

Our sales cycle is unpredictable and lengthy, which makes it difficult to forecast revenue and may increase the magnitude of quarterly fluctuations in our operating results.

The sales cycle for our sequencing instruments is lengthy because they are a major capital item and generally require the approval of our customers' senior management. This may contribute to substantial fluctuations in our quarterly operating results, particularly during the periods in which our sales volume is low. Because of these fluctuations, it is likely that in some future quarters our operating results will fall below the expectations of securities analysts or investors. If that happens, the market price of our stock would likely decrease. Past fluctuations in our quarterly operating results have resulted in decreases in our stock price. Such fluctuations also mean that investors may not be able to rely upon our operating results in any particular period as an indication of future performance.

Our operations involve the use of hazardous materials, and we must comply with environmental, health and safety laws, which can be expensive and may adversely affect our business, operating results and financial condition.

Our research and development and manufacturing activities involve the use of hazardous materials, including chemicals and biological materials, and some of our products include hazardous materials. Accordingly, we are subject to federal, state, local and foreign laws, regulations and permits relating to environmental, health and safety matters, including, among others, those governing the use, storage, handling, exposure to and disposal of hazardous materials and wastes, the health and safety of our employees, and the shipment, labeling, collection, recycling, treatment and disposal of products containing hazardous materials. Liability under environmental laws and regulations can be joint and several and without regard to fault or negligence. For example, under certain circumstances and under certain environmental laws, we could be held liable for costs relating to contamination at our or our predecessors' past or present facilities and at third-party waste disposal sites. We could also be held liable for damages arising out of human exposure to hazardous materials. There can be no assurance that violations of environmental, health and safety laws will not occur as a result of human error, accident, equipment failure or other causes. The failure to comply with past, present or future laws could result in the imposition of substantial fines and penalties, remediation costs, property damage and personal injury claims, investigations, the suspension of production or product sales, loss of permits or a cessation of operations. Any of these events could harm our business, operating results and financial condition. We also expect that our operations will be affected by new environmental, health and safety laws and regulations on an ongoing basis, or more stringent enforcement of existing laws and regulations. New laws or changes to existing laws may result in additional costs and may increase penalties associated with violations or require us to change the content of our products or how we manufacture them, which could have a material adverse effect on our business, operating results and financial condition.

Our facilities in California are located near known earthquake faults, and the occurrence of an earthquake or other catastrophic disaster could cause damage to our facilities and equipment, which could require us to cease or curtail operations.

Our facilities in the San Francisco Bay Area are located near known earthquake fault zones and are vulnerable to damage from earthquakes. We are also vulnerable to damage from other types of disasters, including fire, floods, power loss, communications failures and similar events. If any disaster were to occur, our ability to operate our business at our facilities would be seriously, or potentially completely, impaired. In addition, the nature of our activities could cause significant delays in our research programs and commercial activities and make it difficult for us to recover from a disaster. The insurance we maintain may not be adequate to cover our losses resulting from disasters or other business interruptions. Accordingly, an earthquake or other disaster could materially and adversely harm our

ability to conduct business.

Ethical, legal, privacy and social concerns surrounding the use of genetic information could reduce demand for our technology.

Our products may be used to provide genetic information about humans, agricultural crops and other living organisms. The information obtained from our products could be used in a variety of applications which may have underlying ethical, legal, privacy and social concerns, including the genetic engineering or modification of agricultural products or testing for genetic predisposition for certain medical conditions. Governmental authorities could, for safety, social or other purposes, call for limits on or regulation of the use of genetic testing. Such concerns or governmental restrictions could limit the use of our products, which could have a material adverse effect on our business, financial condition and results of operations.

Disruption of critical information technology systems or material breaches in the security of our systems could harm our business, customer relations and financial condition.

Information technology ("IT") helps us operate efficiently, interface with customers, maintain financial accuracy and efficiency and accurately produce our financial statements. IT systems are used extensively in virtually all aspects of our business, including sales forecast, order fulfillment and billing, customer service, logistics, and management of data from running samples on our products. Our success depends, in part, on the continued and uninterrupted performance of our IT systems. IT systems may be

vulnerable to damage from a variety of sources, including telecommunications or network failures, power loss, natural disasters, human acts, computer viruses, computer denial-of-service attacks, unauthorized access to customer or employee data or company trade secrets, and other attempts to harm our systems. Certain of our systems are not redundant, and our disaster recovery planning is not sufficient for every eventuality. Despite any precautions we may take, such problems could result in, among other consequences, disruption of our operations, which could harm our reputation and financial results.

If we do not allocate and effectively manage the resources necessary to build and sustain the proper IT infrastructure, we could be subject to transaction errors, processing inefficiencies, the loss of customers, business disruptions or the loss of or damage to intellectual property through security breach. If our data management systems do not effectively collect, store, process and report relevant data for the operation of our business, whether due to equipment malfunction or constraints, software deficiencies or human error, our ability to effectively plan, forecast and execute our business plan and comply with applicable laws and regulations will be impaired, perhaps materially. Any such impairment could materially and adversely affect our reputation, financial condition, results of operations, cash flows and the timeliness with which we report our internal and external operating results.

Security breaches and other disruptions could compromise our information and expose us to liability, which would cause our business and reputation to suffer.

In the ordinary course of our business, we collect and store sensitive data, including intellectual property, our proprietary business information and that of our customers, suppliers and business partners, and personally identifiable information of our customers and employees, in our data centers and on our networks. The secure processing, maintenance and transmission of this information is critical to our operations. Despite our security measures, our IT infrastructure may be vulnerable to attacks by hackers or breached due to employee error, malfeasance, faulty password management or other disruptions. Third parties may attempt to fraudulently induce employees or other persons into disclosing user names, passwords or other sensitive information, which may in turn be used to access our IT systems. Any such breach could compromise our networks and the information stored there could be accessed, publicly disclosed, lost or stolen. Any such access, disclosure or other loss of information could result in legal claims or proceedings, liability under laws that protect the privacy of personal information, disruption of our operations and damage to our reputation, which could adversely affect our business, revenues and competitive position.

Regulations related to conflict minerals will cause us to incur additional expenses and could limit the supply and increase the costs of certain materials used in the manufacture of our products.

We are subject to requirements under the Dodd-Frank Wall Street Reform and Consumer Protection Act of 2010, or the Dodd-Frank Act, that require us to conduct diligence, and report whether or not our products contain conflict minerals. The implementation of these requirements could adversely affect the sourcing, availability and pricing of the materials used in the manufacture of components used in our products. Furthermore, the complex nature of our products requires components and materials that may be available only from a limited number of sources and, in some cases, from only a single source. We have incurred, and will continue to incur, additional costs to comply with the disclosure requirements, including costs related to conducting diligence procedures to determine the sources of conflict minerals that may be used or necessary to the production of our products and, if applicable, potential changes to components, processes or sources of supply as a consequence of such verification activities. We may face reputational harm if we determine that certain of our instruments contain minerals not determined to be conflict free or if we are unable to alter our processes or sources of supply to avoid using such materials. Reputational harm could adversely affect our business, financial condition or results of operations.

Risks Related to Our Intellectual Property

Failure to secure patent or other intellectual property protection for our products and improvements to our products may reduce our ability to maintain any technological or competitive advantage over our competitors and potential competitors.

Our ability to protect and enforce our intellectual property rights is uncertain and depends on complex legal and factual questions. Our ability to establish or maintain a technological or competitive advantage over our competitors may be diminished because of these uncertainties. For example:

- we or our licensors might not have been the first to make the inventions covered by each of our pending patent applications or issued patents;
- we or our licensors might not have been the first to file patent applications for these inventions;
- it is possible that neither our pending patent applications nor the pending patent applications of our licensors will result in issued patents;
- our patents or the patents of our licensors may not be of sufficient scope to prevent others from practicing our technologies, developing competing products, designing around our patented technologies or independently developing similar or alternative technologies;

- our and our licensors' patent applications or patents have been, are and may in the future be, subject to interference, opposition or similar administrative proceedings, which could result in those patent applications failing to issue as patents, those patents being held invalid or the scope of those patents being substantially reduced;
- we or our partners may not adequately protect our trade secrets;
- we may not develop additional proprietary technologies that are patentable; or
- the patents of others may limit our freedom to operate and prevent us from commercializing our technology in accordance with our plans.

The occurrence of any of these events could impair our ability to operate without infringing upon the proprietary rights of others or prevent us from establishing or maintaining a competitive advantage over our competitors.

Variability in intellectual property laws may adversely affect our intellectual property position.

Intellectual property laws, and patent laws and regulations in particular, have been subject to significant variability either through administrative or legislative changes to such laws or regulations or changes or differences in judicial interpretation, and it is expected that such variability will continue to occur. Additionally, intellectual property laws and regulations differ among countries. Variations in the patent laws and regulations or in interpretations of patent laws and regulations in the United States and other countries may diminish the value of our intellectual property and may change the impact of third-party intellectual property on us. Accordingly, we cannot predict the scope of patents that may be granted to us, the extent to which we will be able to enforce our patents against third parties or the extent to which third parties may be able to enforce their patents against us.

Some of the intellectual property that is important to our business is owned by other companies or institutions and licensed to us, and changes to the rights we have licensed may adversely impact our business.

We license from third parties some of the intellectual property that is important to our business. If we fail to meet our obligations under these licenses, these third parties could terminate the licenses. If the third parties who license intellectual property to us fail to maintain the intellectual property that we have licensed, or lose rights to that intellectual property, the rights we have licensed may be reduced or eliminated, which could subject us to claims of intellectual property infringement. Termination of these licenses or reduction or elimination of our licensed rights may result in our having to negotiate new or reinstated licenses with less favorable terms, or could subject us to claims of intellectual property infringement in litigation or other administrative proceedings that could result in damage awards against us and injunctions that could prohibit us from selling our products. In addition, some of our licenses from third parties limit the field in which we can use the licensed technology. Therefore, in order for us to use such licensed technology in potential future applications that are outside the licensed field of use, we may be required to negotiate new licenses with our licensors or expand our rights under our existing licenses. We cannot assure you that we will be able to obtain such licenses or expanded rights on reasonable terms or at all. In addition, we have limited rights to participate in the prosecution and enforcement of the patents and patent applications that we have licensed. As a result, we cannot be certain that these patents and applications will be prosecuted and enforced in a manner consistent with the best interests of our business. Further, because of the rapid pace of technological change in our industry, we may need to rely on key technologies developed or licensed by third parties, and we may not be able to obtain licenses and technologies from these third parties at all or on reasonable terms. The occurrence of these events may have a material adverse effect on our business, financial condition or results of operations.

The measures that we use to protect the security of our intellectual property and other proprietary rights may not be adequate, which could result in the loss of legal protection for, and thereby diminish the value of, such intellectual

property and other rights.

In addition to patents, we also rely upon trademarks, trade secrets, copyrights and unfair competition laws, as well as license agreements and other contractual provisions, to protect our intellectual property and other proprietary rights. Despite these measures, any of our intellectual property rights could be challenged, invalidated, circumvented or misappropriated. In addition, we attempt to protect our intellectual property and proprietary information by requiring our employees and consultants to enter into confidentiality and assignment of inventions agreements, and by entering into confidentiality agreements with our third-party development, manufacturing, sales and distribution partners, who may also acquire, develop and/or commercialize alternative or competing products or provide services to our competitors. For example, Roche has certain access to our trade secrets and other proprietary information pursuant to the Roche Agreement, subject to the confidentiality provisions thereof; however, Roche has also developed and commercializes its 454 Life Sciences sequencing systems and is developing alternative and potentially competing sequencing products through its recent acquisition of Genia Technologies. There can be no assurance, however, that such measures will provide adequate protection for our intellectual property and proprietary information. These agreements may be breached, and we may not have adequate remedies for any such breach. In addition, our trade secrets and other proprietary information may be disclosed to others, or others may gain access to or disclose our trade secrets and other proprietary information. Enforcing a claim that a third party illegally obtained and is using our trade secrets is expensive and time consuming, and the outcome is unpredictable. Additionally, others may independently develop proprietary information and techniques that are substantially equivalent to ours. The occurrence of these events may have a material adverse effect on our business, financial condition or results of operations.

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Our intellectual property may be subject to challenges in the United States or foreign jurisdictions that could adversely affect our intellectual property position.

Our pending, issued and granted U.S. and foreign patents and patent applications have been, are and may in the future be, subject to challenges by third parties asserting prior invention by others or invalidity on various grounds, through proceedings, such as interferences, reexamination or opposition proceedings. Addressing these challenges to our intellectual property has previously been, and any future challenges can be, costly and distract management's attention and resources. For example, we previously incurred significant legal expenses to litigate and settle a complaint seeking review of a patent interference decision of the U.S. Patent and Trademark Office. Additionally, as a result of these challenges, our patents or pending patent applications may be determined to be unpatentable to us, invalidated or unenforceable in whole or in part. Accordingly, adverse rulings from the relevant patent offices in these proceedings may negatively impact the scope of our intellectual property protection for our products and technology and may adversely affect our business.

Some of our technology is subject to "march-in" rights by the U.S. government.

Some of our patented technology was developed with U.S. federal government funding. When new technologies are developed with U.S. government funding, the government obtains certain rights in any resulting patents, including a nonexclusive license authorizing the government to use the invention for non-commercial purposes. These rights may permit the government to disclose our confidential information to third parties and to exercise "march-in" rights to use or allow third parties to use our patented technology. The government can exercise its march-in rights if it determines that action is necessary because we fail to achieve practical application of the U.S. government-funded technology, because action is necessary to alleviate health or safety needs, to meet requirements of federal regulations, or to give preference to U.S. industry. In addition, U.S. government-funded inventions must be reported to the government and U.S. government funding must be disclosed in any resulting patent applications. In addition, our rights in such inventions are subject to government license rights and foreign manufacturing restrictions.

We may become involved in legal proceedings to enforce our intellectual property rights.

Our intellectual property rights involve complex factual, scientific and legal questions. We operate in an industry characterized by significant intellectual property litigation. Even though we may believe that we have a valid patent on a particular technology, other companies may have from time to time taken, and may in the future take, actions that we believe violate our patent rights. Legal actions to enforce these patent rights can be expensive and may involve the diversion of significant management time and resources. Our enforcement actions may not be successful, could give rise to legal claims against us and could result in some of our intellectual property rights being determined to be invalid or not enforceable.

We could in the future be subject to legal proceedings with third parties who may claim that our products infringe or misappropriate their intellectual property rights.

Our products are based on complex, rapidly developing technologies. We may not be aware of issued or previously filed patent applications belonging to third parties that mature into issued patents that cover some aspect of our products or their use. In addition, because patent litigation is complex and the outcome inherently uncertain, our belief that our products do not infringe third-party patents of which we are aware or that such third-party patents are invalid and unenforceable may be determined to be incorrect. As a result, third parties have claimed, and may in the future claim, that we infringe their patent rights and have filed, and may in the future file, lawsuits or engage in other proceedings against us to enforce their patent rights. In addition, as we enter new markets, our competitors and other third parties may claim that our products infringe their intellectual property rights as part of a business strategy to impede our successful entry into those markets. Patent litigation between competitors in our industry is common.

Additionally, we have certain obligations to many of our customers to indemnify and defend them against claims by third parties that our products or their use infringe any intellectual property of these third parties. In defending ourselves against any of these claims, we have in the past incurred, and could in the future incur, substantial costs, and the attention of our management and technical personnel could be diverted. For example, we previously incurred significant legal expenses to litigate and settle a complaint alleging patent infringement. Even if we have an agreement to indemnify us against such costs, the indemnifying party may be unable to uphold its contractual obligations. To avoid or settle legal claims, it may be necessary or desirable in the future to obtain licenses relating to one or more products or relating to current or future technologies, which could negatively affect our gross margins. We may not be able to obtain these licenses on commercially reasonable terms, or at all. We may be unable to modify our products so that they do not infringe the intellectual property rights of third parties. In some situations the results of litigation or settlement of claims may require that we cease allegedly infringing activities which could prevent us from selling some or all of our products. The occurrence of these events may have a material adverse effect on our business, financial condition or results of operations.

In addition, in the course of our business we may from time to time have access or be alleged to have access to confidential or proprietary information of others, which though not patented, may be protected as trade secrets. Others could bring claims against us asserting that we improperly used their confidential or proprietary information, or misappropriated their technologies and incorporated those technologies into our products. A determination that we illegally used the confidential or proprietary information or misappropriated technologies of others in our products could result in our having to pay substantial damage awards or be prevented from selling some or all of our products, which could adversely affect our business.

We have not yet registered some of our trademarks in all of our potential markets, and failure to secure those registrations could adversely affect our business.

Some of our trademark applications may not be allowed for registration, and our registered trademarks may not be maintained or enforced. In addition, in the U.S. Patent and Trademark Office and in comparable agencies in many foreign jurisdictions, third parties are given an opportunity to oppose pending trademark applications and to seek to cancel registered trademarks. Opposition or cancellation proceedings may be filed against our trademarks, and our trademarks may not survive such proceedings.

Our use of “open source” software could adversely affect our ability to sell our products and subject us to possible litigation.

A portion of our products or technologies developed and/or distributed by us incorporate “open source” software, and we may incorporate open source software into other products or technologies in the future. Some open source software licenses require that we disclose the source code for any modifications to such open source software that we make and distribute to one or more third parties, and that we license the source code for such modifications to third parties, including our competitors, at no cost. We monitor the use of open source software in our products to avoid uses in a manner that would require us to disclose or grant licenses under our source code that we wish to maintain as proprietary, however there can be no assurance that such efforts have been or will be successful. In some circumstances, distribution of our software that includes or is linked with open source software could require that we disclose and license some or all of our proprietary source code in that software, which could include permitting the use of such software and source code at no cost to the user. Open source license terms are often ambiguous, and there is little legal precedent governing the interpretation of these licenses. Successful claims made by the licensors of open source software that we have violated the terms of these licenses could result in unanticipated obligations including being subject to significant damages, being enjoined from distributing products that incorporate open source software, and being required to make available our proprietary source code pursuant to an open source license, which could substantially help our competitors develop products that are similar to or better than ours and otherwise adversely affect our business.

Risks Related to Owning Our Common Stock

The price of our common stock has been, is, and may continue to be, highly volatile, and you may be unable to sell your shares at or above the price you paid to acquire them.

The market price of our common stock is highly volatile, and we expect it to continue to be volatile for the foreseeable future in response to many risk factors listed in this section, and others beyond our control, including:

- actual or anticipated fluctuations in our financial condition and operating results;
- announcements of technological innovations by us or our competitors;
- announcements by our customers, partners or suppliers relating directly or indirectly to our products, services or technologies;
- overall conditions in our industry and market;
- addition or loss of significant customers;
- changes in laws or regulations applicable to our products;

- actual or anticipated changes in our growth rate relative to our competitors;
- announcements by us or our competitors of significant acquisitions, strategic partnerships, joint ventures, capital commitments or achievement of significant milestones;
- additions or departures of key personnel;
- competition from existing products or new products that may emerge;
- issuance of new or updated research or reports by securities analysts;
- fluctuations in the valuation of companies perceived by investors to be comparable to us;
- disputes or other developments related to proprietary rights, including patents, litigation matters and our ability to obtain intellectual property protection for our technologies;
- announcement or expectation of additional financing efforts;
- sales of our common stock by us or our stockholders;
- stock price and volume fluctuations attributable to inconsistent trading volume levels of our shares;
- reports, guidance and ratings issued by securities or industry analysts; and
- general economic and market conditions.

If any of the forgoing occurs, it would cause our stock price or trading volume to decline. Stock markets in general and the market for companies in our industry in particular have experienced price and volume fluctuations that have affected and continue to

affect the market prices of equity securities of many companies. These fluctuations often have been unrelated or disproportionate to the operating performance of those companies. These broad market and industry fluctuations, as well as general economic, political and market conditions such as recessions, interest rate changes or international currency fluctuations, may negatively impact the market price of our common stock. You may not realize any return on your investment in us and may lose some or all of your investment. In the past, companies that have experienced volatility in the market price of their stock have been subject to securities class action litigation. We have been a party to this type of litigation in the recent past and may be the target of this type of litigation again in the future. Securities litigation against us could result in substantial costs and divert our management's attention from other business concerns, which could seriously harm our business.

Future sales of our common stock could cause our stock price to fall.

We maintain a shelf registration statement on Form S-3 with the SEC pursuant to which we may, from time to time, sell up to an aggregate of \$150 million of our common stock, preferred stock, depositary shares, warrants, units or debt securities. We have established, and may in the future establish, "at-the-market" offerings pursuant to which we may offer and sell shares of our common stock. Sales of securities under the registration statement will result in dilution of our stockholders and could cause our stock price to fall.

In addition, the holders of a significant number of shares of our common stock are entitled to rights with respect to registration of such shares under the Securities Act pursuant to an investor rights agreement between such holders and us. If such holders, by exercising their registration rights, sell a large number of shares, they could adversely affect the market price for our common stock. If we file a registration statement for the purpose of selling additional shares to raise capital and are required to include shares held by these holders pursuant to the exercise of their registration rights, our ability to raise capital may be impaired. Such holders have waived their registration rights with respect to the sale of shares of our common stock pursuant to the registration statements on Form S-3.

Concentration of ownership by our principal stockholders may result in control by such stockholders of the composition of our board of directors.

Our existing significant stockholders, executive officers, directors and their affiliates beneficially own a significant number of our outstanding shares of common stock. As a result, these stockholders will be able to exercise a significant level of control over all matters requiring stockholder approval, including the election of directors. This control could have the effect of delaying or preventing a change of control of our company or changes in management and will make the approval of certain transactions difficult or impossible without the support of these stockholders.

Anti-takeover provisions in our charter documents and under Delaware law could make an acquisition of us, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management and limit the market price of our common stock.

Provisions in our certificate of incorporation and bylaws, as amended and restated, may have the effect of delaying or preventing a change of control or changes in our management. Our amended and restated certificate of incorporation and bylaws include provisions that:

- authorize our board of directors to issue, without further action by the stockholders, up to 50,000,000 shares of undesignated preferred stock and up to approximately 1,000,000,000 shares of authorized but unissued shares of common stock;
- require that any action to be taken by our stockholders be effected at a duly called annual or special meeting and not by written consent;

- specify that special meetings of our stockholders can be called only by our board of directors, the Chairman of the Board, the Chief Executive Officer or the President;
- establish an advance notice procedure for stockholder approvals to be brought before an annual meeting of our stockholders, including proposed nominations of persons for election to our board of directors;
- establish that our board of directors is divided into three classes, Class I, Class II and Class III, with each class serving staggered terms;
- provide that our directors may be removed only for cause; and
- provide that vacancies on our board of directors may be filled only by a majority of directors then in office, even though less than a quorum.

These provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors, which is responsible for appointing the members of our management. In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which limits the ability of stockholders owning in excess of 15% of our outstanding voting stock to merge or combine with us.

Our development agreement with Roche may deter or reduce the number of potential acquirers thus reducing or placing negative pressure on our stock price.

The Roche Agreement could make an acquisition of our company, which may be beneficial to our stockholders, less likely, whether or not we realize the expected benefits from the Roche Agreement. For example, the exclusive rights and licenses granted to Roche pursuant to the Roche Agreement, or our development, manufacturing and supply obligations pursuant to the Roche Agreement, may make an acquisition of our company less appealing to third parties that compete with Roche.

Our large number of authorized but unissued shares of common stock may potentially dilute your stockholdings.

We have a significant number of authorized but unissued shares of common stock. Our board of directors may issue shares of common stock from this authorized but unissued pool from time to time without stockholder approval, resulting in the dilution of our existing stockholders.

We do not intend to pay dividends for the foreseeable future.

We have never declared or paid any cash dividends on our common stock and do not intend to pay any cash dividends in the foreseeable future. In addition, the terms of our existing debt agreement restrict our ability to pay dividends on our common stock. We anticipate that we will retain all of our future earnings for use in the operation of our business and for general corporate purposes. Any determination to pay dividends in the future will be at the discretion of our board of directors. Accordingly, investors must rely on sales of their common stock after price appreciation, which may never occur, as the only way to realize any future gains on their investments.

ITEM 1B.UNRESOLVED STAFF COMMENTS

None.

ITEM 2.PROPERTIES

As of December 31, 2014, we leased approximately 186,000 square feet in Menlo Park, California, where we house our headquarters, research and development, service and support functions, and our in-house manufacturing operations. Our leases run through 2015 with certain options for renewal. We also lease a sales office facility in Singapore and an engineering support facility in San Francisco. We believe that our existing facilities, together with suitable additional or alternative space available on commercially reasonable terms, will be sufficient to meet our needs.

As mentioned above, our Menlo Park facility leases expire in December 2015. Furthermore, our previous landlord sold the Menlo Park property in February 2015. We have entered into discussions with the new landlord regarding our right to exercise the five-year extension options as well as other alternatives. To facilitate the on-going conversations and in consideration of our agreement to delay exercising the extension options, the landlord agreed to a 50% reduction in the monthly base rent payable under the leases for each of the months of January, February and March 2015, as we continue to negotiate terms for our new leases.

ITEM 3.LEGAL PROCEEDINGS

From time to time, we may be involved in a variety of claims, lawsuits, investigations and proceedings relating to securities laws, product liability, patent infringement, contract disputes and other matters relating to various claims that arise in the normal course of our business. We do not know whether we will prevail in these matters nor can we assure that any remedy could be reached on commercially reasonable terms, if at all. Regardless of the outcome, litigation can have an adverse impact on us because of defense and settlement costs, diversion of management resources and other factors. Based on currently available information, we believe that we have meritorious defenses to these actions and that the resolution of these cases is not likely to have a material adverse effect on our business, financial position or future results of operations.

ITEM 4.MINE SAFETY DISCLOSURES

Not applicable.

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PART II

ITEM 5. MARKET FOR REGISTRANT’S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES

Our common stock is being traded in The Nasdaq Global Select Market under the symbol “PACB.” The following table sets forth the high and low closing sales prices per share for our common stock for the indicated fiscal periods:

	2014		2013	
	High	Low	High	Low
4th Quarter	\$ 8.10	\$ 4.52	\$ 5.95	\$ 3.47
3rd Quarter	6.42	4.38	6.50	2.45
2nd Quarter	6.65	3.87	2.94	1.95
1st Quarter	8.20	4.73	3.25	1.60

Holders of Record

As of March 3, 2015, there were approximately 49 stockholders of record of our common stock, although we believe that there are a significantly larger number of beneficial owners of our common stock.

Dividend Policy

We have never declared or paid any cash dividend on our common stock and have no present plans to do so. We intend to retain earnings for use in the operation and expansion of our business. In addition, our ability to pay dividends is limited pursuant to covenants in our debt agreements.

Securities Authorized for Issuance under Equity Compensation Plans

The following table contains information as of December 31, 2014 for our equity compensation plans.

Number of securities to be issued upon exercise	Weighted-average exercise price of	Number of securities remaining available for future issuance under compensation plans
-------------------------------------------------	------------------------------------	---------------------------------------------------------------------------------------

Plan category	of outstanding options, warrants and rights (a)	outstanding options, warrants and rights	(excluding securities reflected in column(a))
Equity compensation plans approved by security holders	16,491,164	\$ 5.10	4,944,805
Equity compensation plans not approved by security holders	—	—	—

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Performance Graph

The performance graph included in this Form 10-K shall not be deemed “filed” for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the “Exchange Act”), or incorporated by reference into any filing of Pacific Biosciences under the Securities Act of 1933, as amended, or the Exchange Act, except as shall be expressly set forth by specific reference in such filing.

The following graph shows a comparison from October 27, 2010 (the date our common stock commenced trading on the Nasdaq Global Select Market) through December 31, 2014 of the cumulative total return for our common stock, the Nasdaq Composite Index and the Nasdaq Biotechnology Index. Such returns are based on historical results and are not intended to suggest future performance. Data for The Nasdaq Composite Index and the Nasdaq Biotechnology Index assume reinvestment of dividends.

	October 27, 2010	December 31, 2010	December 31, 2011	December 31, 2012	December 31, 2013	December 31, 2014
Pacific Biosciences of California, Inc.	\$ 100.00	\$ 96.78	\$ 17.03	\$ 10.34	\$ 31.81	\$ 47.69
NASDAQ Composite Index	100.00	105.63	106.07	123.83	175.47	200.78
NASDAQ Biotechnology Index	100.00	101.49	114.21	152.38	259.25	358.99

Recent Sales of Unregistered Securities

None.

Use of Proceeds

On October 5, 2012, we entered into a sales agreement pursuant to which we were permitted to offer and sell, from time to time, shares of our common stock having an aggregate offering price of up to \$30.0 million through an “at-the-market” offering. On November 8, 2013, the sales agreement was amended to increase the shares of our common stock that may be sold pursuant to the sales agreement by an additional aggregate offering price of \$30.0 million. On February 3, 2015, the sales agreement was amended again in order to increase the shares of our common stock that may be sold pursuant to the sales agreement, and we are currently permitted to sell our common stock up to an additional aggregate offering price of \$30.0 million under the sales agreement. We pay a commission equal to 3% of the gross proceeds from the sale of shares of our common stock under the sales agreement. We intend to

use the net proceeds from this offering for general corporate purposes, including capital expenditures, debt repayments and working capital. 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. We are not obligated to make any sales of shares of our common stock under the sales agreement. As of December 31, 2014, we have sold a total of 14.1 million shares of our common stock at an average price of \$4.27 through our “at-the-market” offering, for total net proceeds of \$58.0 million.

ITEM 6. SELECTED FINANCIAL DATA

Our historical results are not necessarily indicative of the results to be expected for any future period. The following selected financial data should be read in conjunction with “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and our consolidated financial statements and related notes included elsewhere in this Form 10-K.

	Year Ended December 31,				
	2014	2013	2012	2011	2010
	(in thousands except per share amounts)				
Total revenue (1)(2)	\$ 60,594	\$ 28,181	\$ 25,983	\$ 33,863	\$ 1,674
Total cost of revenue (1)	37,192	21,762	25,043	20,829	—
Gross profit (1)	23,402	6,419	940	13,034	1,674
Total operating expense	86,256	83,962	95,278	122,790	141,908
Operating loss	(62,854)	(77,543)	(94,338)	(109,756)	(140,234)
Net loss	\$ (66,160)	\$ (79,293)	\$ (94,465)	\$ (109,388)	\$ (140,166)
Net loss per share:					
Basic and diluted net loss per share	\$ (0.94)	\$ (1.26)	\$ (1.69)	\$ (2.03)	\$ (14.10)
Shares used in computing basic and diluted net loss per share (3)	70,475	62,784	55,733	53,874	9,938
	As of December 31,				
	2014	2013	2012	2011	2010
	(in thousands)				
Cash, cash equivalents and investments	\$ 101,348	\$ 112,528	\$ 100,580	\$ 177,434	\$ 283,674
Working capital	86,271	103,904	100,257	180,225	272,274
Total assets	124,523	136,185	129,683	218,316	305,747
Total liabilities (4)	69,574	67,005	20,301	26,853	25,881
Total stockholders' equity (deficit) (3)	\$ 54,949	\$ 69,180	\$ 109,382	\$ 191,463	\$ 279,866

(1) We began recording product and service revenue and the related cost of revenue in 2011 from sales of our PacBio RS instruments and consumables. Prior to 2011, our revenue and gross profit consisted solely of grant revenue. Prior to 2012, cost of revenue and gross profit do not reflect certain costs, as instrument components

acquired prior to September 30, 2010 were expensed as period costs.

- (2) During 2013 we entered into a Development, Commercialization and License Agreement (the “Roche Agreement”) with F. Hoffman-La Roche Ltd (“Roche”) and received a non-refundable up-front payment of \$35.0 million. Revenue for the year ended December 31, 2014 consists of four quarterly amortization of \$1.7 million from the non-refundable up-front payment of \$35.0 million, and our achievement of a \$10.0 million milestone pursuant to the Roche Agreement, with the remaining \$26.5 million deferred and to be amortized as revenue over the estimated obligation periods. Please see “Note 3. Contractual Revenue” in Part II, Item 8 of this Form 10-K for additional information.
- (3) During 2012, we entered into a sales agreement pursuant to which we were permitted to offer and sell, from time to time, shares of our common stock having an aggregate offering price of up to \$30.0 million through an at-the-market offering. On November 7, 2013, the sales agreement was amended to permit us to raise an additional \$30.0 million through an at-the-market offering. On February 3, 2015, the sales agreement was amended again in order to increase the shares of our common stock that may be sold through an at-the-market offering pursuant to the sales agreement. In the year ended December 31, 2014, we issued 5.8 million shares of our common stock at an average price of \$6.81 per share through our “at-the-market” offering.

- (4) During 2013 we entered into a debt agreement pursuant to which we received \$20.5 million in funding and issued promissory notes in the aggregate principal amount of \$20.5 million and warrants to purchase 5,500,000 shares of our common stock. Please see “Note 6. Notes payable” in Part II, Item 8 of this Form 10-K for additional information.

ITEM 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

You should read the following discussion and analysis of our financial condition and results of operations together with our consolidated financial statements and the related notes included in this Form 10-K. Some of the information contained in this discussion and analysis or set forth elsewhere in this Form 10-K, including information with respect to our plans and strategy for our business and related financing, includes forward-looking statements that involve risks and uncertainties. You should read the "Risk Factors" section of this Form 10-K for a discussion of important factors that could cause actual results to differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

Overview

We design, develop and manufacture the PacBio® RS II Sequencing System to help scientists resolve genetically complex problems. Based on our novel Single Molecule, Real-Time (SMRT®) technology, our products enable: de novo genome assembly to finish genomes in order to more fully identify, annotate and decipher genomic structures; full-length transcript analysis to improve annotations in reference genomes, characterize alternatively spliced isoforms and find novel genes; targeted sequencing to more comprehensively characterize genetic variations; and DNA base modification identification to help characterize epigenetic regulation and DNA damage. Our technology combines very high consensus accuracy and long read lengths with the ability to detect real-time kinetic information.

2014 Business Events and Trends

Bookings and Revenue Growth. During the year ended December 31, 2014, we achieved stronger instrument sales and accepted orders for 40 instruments, compared to 25 during 2013, ending 2014 with 15 in backlog. We attribute the stronger bookings largely to increased customer awareness of the expanding applications for SMRT Sequencing, and the improved reliability and performance of our instruments. We generally expect installation of new instruments to occur one to two quarters after they are booked. Revenue during 2014 was \$60.6 million dollars, up 115% over revenue of \$28.2 million recognized during the year ended December 31, 2013. The revenue increase year-over-year stemmed from substantial increases in all categories, including sales of instruments, consumables, service and other revenue, and a \$15.1 million increase in contractual revenue. Revenue can fluctuate on a quarterly basis, which in some cases may be attributable to seasonal fluctuations.

Product Enhancements. During 2014, we continued to significantly enhance the performance of the PacBio RS II System, which includes the PacBio RS II instrument, consumables and software, through a combination of sample preparation protocol enhancements, software releases, and the release of a new sequencing reagent chemistry. By providing an increasing number of longer reads per instrument run, the new sequencing reagent chemistry enables users to assemble more genomes to a high quality. We have continually improved our software to expand the number of supported applications such as large genome assembly, sequencing of transcript isoforms produced from genes, and phasing of haplotypes in large amplicons. During 2015 we plan to further improve our existing products, including chemistry and sample preparation improvements to increase throughput and expand our supported applications, and to develop new products.

Diagnostic Collaboration with Roche. During the third quarter of 2013 we entered into a Development, Commercialization and License Agreement (the "Roche Agreement") with F. Hoffman-La Roche Ltd ("Roche"), whereby we received a nonrefundable up-front payment of \$35 million. The Roche Agreement also provides for our ability to receive additional payments totaling up to \$40 million, subject to our achievement of certain milestones. During 2014, we recognized ongoing revenue of \$6.8 million from the up-front payment and also achieved our first milestone under the Roche Agreement, for which we received \$10 million during the third quarter of 2014, leaving a remaining \$30

million in potential milestone payments. We expect to earn another \$10 million in milestone revenue during 2015; however, achievement of future milestones is not assured. During 2015, we also expect to continue recognizing revenue from the up-front payment.

Cash Position. For the year ended December 31, 2014, our balance of cash, cash equivalents and investments totaled \$101.3 million, reflecting a decrease of \$11.2 million from the prior year, primarily reflecting our net loss of \$66.2 million, less \$14.2 million non-cash expenses for stock compensation expense and depreciation. During 2014, we also raised \$38.0 million through the sale of common stock under our “at-the-market” offering. We plan to raise additional capital in the future. To the extent we raise additional funds through the issuance of equity, such issuance will result in dilution to our stockholders. Our cash position is dependent on our revenue, including timing of contractual revenue as well as any additional funds raised.

Critical Accounting Policies and Estimates

Management’s Discussion and Analysis of Financial Condition and Results of Operations is based upon our Consolidated Financial Statements, which we have prepared in accordance with U.S. generally accepted accounting principles (“GAAP”). The preparation of these financial statements requires management to make estimates and assumptions that affect the reported amounts of assets, liabilities, revenue, cost of revenue, and operating expenses, and related disclosure of contingent assets and liabilities. Management based its estimates on historical experience and on various other assumptions that it believes to be reasonable under the

circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ materially from these estimates under different assumptions or conditions.

An accounting policy is deemed to be critical if it requires an accounting estimate to be made based on assumptions about matters that are highly uncertain at the time the estimate is made, if different estimates reasonably could have been used, or if changes in the estimate that are reasonably likely to occur could materially impact the financial statements.

Revenue Recognition

Our revenue is generated primarily from the sale of products and services, in addition to revenue from collaboration agreements. Product revenue consists of sales of our instruments and related consumables; Service and other revenue primarily consist of revenue earned from product maintenance agreements and grant revenue. Contractual revenue relates to revenue recognized from the collaboration agreement under which we received an upfront fee and may receive contingent milestone payments. Our deliverables under the arrangement includes licenses to intellectual property rights and research and development services.

We recognize revenue when persuasive evidence of an arrangement exists, delivery has occurred or services have been rendered, the price is fixed or determinable, and collectability is reasonably assured. For instances where final acceptance of the product or system is required, revenue is deferred until all acceptance criteria have been met. Revenue for product sales is generally recognized upon customer acceptance. Revenue for product maintenance agreements is recognized when earned, which is generally ratably over the service period. In order to assess whether the price is fixed or determinable, we evaluate whether refund rights exist. If refund rights exist or payment terms are based on future performance, we defer revenue recognition until the price becomes fixed or determinable. We assess collectability based on a number of factors, including customer creditworthiness. If we determine that collection of amounts due is not reasonably assured, revenue recognition is deferred until receipt of payment.

We regularly enter into arrangements, comprised of one or more contracts, from which revenue is derived from multiple deliverables including a mix of products and or services. Revenue recognition for contracts with multiple deliverables is based on the individual units of accounting determined to exist in the contract. A delivered item is considered a separate unit of accounting when (i) the delivered item has value to the customer on a stand-alone basis; and (ii) if a general right of return exists, the delivery or performance of an undelivered item is considered probable and under our control. Items are considered to have stand-alone value when they are sold separately by any vendor or when the customer could resell the item on a stand-alone basis. Our revenue arrangements generally do not have a general right of return. When a deliverable does not meet the criteria to be considered a separate unit of accounting, we group it with other deliverables that, when combined, meet the criteria, and the appropriate allocation of arrangement consideration and revenue recognition is determined. Consideration is allocated at the inception of the contract to all deliverables based on their relative selling price. In order to determine the relative selling price of a deliverable, we apply, in order, vendor-specific objective evidence (“VSOE”); third-party evidence if VSOE is not available; and lastly our best estimate of selling price for the deliverable if neither VSOE nor third-party evidence is available.

In order to establish VSOE, we must regularly sell the product or service on a standalone basis with a substantial majority of sales priced within a relatively narrow range. If an insufficient number of standalone sales exist and VSOE cannot be determined, we then consider whether third party evidence can be used to establish selling price. Due to the lack of similar products and services sold by other companies within our industry, we have not established selling

price using third-party evidence. If neither VSOE nor third party evidence of selling price exists, we determine our best estimate of selling price using a combination of prices set by our pricing committee adjusted for applicable discounts and customer orders received to date.

For our collaboration agreement, the process for determining estimates of selling prices of the identifiable deliverables involves significant judgments and estimates to be made by management. Our process considers multiple factors such as estimated headcount, annual research and development budget, estimated length of the research and development period and estimated transfer price on cost, which may vary over time, depending upon the circumstances, and are specific to each deliverable. If the estimated obligation period of one or more deliverables should change, the future amortization of the revenue would also change.

Deferred service revenue primarily represents product maintenance agreement revenue that is expected to be recognized over the related service period, generally one to three years.

We adopted the milestone method as our accounting policy election and recognize milestone revenues as they become earned. Based on Accounting Standards Codification, or ASC, Topic 605-28, Revenue Recognition — Milestone Method, we evaluate contingent milestones at inception of the agreement, and recognize consideration that is contingent upon the achievement of a milestone in its entirety as revenue in the period in which the milestone is achieved only if the milestone is considered substantive in its entirety. Milestones are considered substantive if the consideration earned from the achievement of the milestone (i) is consistent with performance required to achieve the milestone or the increase in value to the delivered item, (ii) relates solely to past performance and (iii) is reasonable relative to all of the other deliverables and payments within the arrangement.

Cost of Revenue

Cost of revenue reflects the direct cost of product components, third-party manufacturing services and our internal manufacturing overhead and customer service infrastructure costs incurred to produce, deliver, maintain and support our instruments, consumables, and services. There are no incremental costs associated with our contractual revenue; all product development costs are reflected in research and development expense.

Manufacturing overhead is predominantly comprised of labor costs. We determine and capitalize manufacturing overhead into inventory based on a standard cost model that approximates actual costs. Prior to achieving manufacturing volumes that correlated with our estimated normal capacity (the production levels expected to be achieved over a number of periods under normal circumstances with available resources), we based our capitalized overhead relative to our normal capacity. Prior to achieving normal capacity, excess manufacturing resources were engaged in research and development activities, including; next generation products, internal use research products, and general support activities. As such, manufacturing costs in excess of amounts reflected in inventory were expensed as a component of research and development expense. During 2014, manufacturing volumes trended towards and then approximated normal capacity, and excess manufacturing resources contributing to research and development activities declined significantly.

Service costs include the direct costs of components used in support, repair and maintenance of customer instruments as well as the cost of personnel, materials, shipping and support infrastructure necessary to support the installed customer base. Prior to the fourth quarter of 2013, the capacity of our existing service infrastructure exceeded the number of installed customer instruments. Therefore, management estimated the capacity of the existing service infrastructure and recognized the service-related cost of revenue based on the installed base. As a result, prior to the fourth quarter of 2013, total service infrastructure costs exceeded the costs associated with the support of customer instruments and such excess costs were included as a component of sales, general and administrative expense.

Stock-Based Compensation

Stock-based compensation expense for all stock-based compensation awards is based on the grant date fair value estimated using the Black-Scholes option pricing model. We have limited historical information available to support the underlying estimates of certain assumptions required to value stock options. The expected term of options is estimated based on the simplified method. We do not have sufficient trading history to solely rely on the volatility of our own common stock for establishing expected volatility. Therefore, we based our expected volatility on the historical stock volatilities of our common stock as well as several comparable publicly listed companies over a period equal to the expected term of the options. The risk-free interest rate is based on the U.S. Treasury yield curve in effect at the time of grant for the expected term of the stock option. We estimate our forfeiture rate based on an analysis of our actual forfeitures and will continue to evaluate the adequacy of the forfeiture rate based on actual forfeiture experience, analysis of employee turnover behavior and other factors. The impact from a forfeiture rate adjustment will be recognized in full in the period of adjustment, and if the actual number of future forfeitures differs from that estimated, we may be required to record adjustments to stock-based compensation expense in future periods. We recognize compensation expense on a straight-line basis over the requisite service period. We elected to use the simplified method to calculate the beginning pool of excess tax benefits.

The assumptions used in calculating the fair value of share-based payment awards represent management's best estimates, but these estimates involve inherent uncertainties and the application of management judgment. As a result, if factors change and we use different assumptions, our stock-based compensation expense could be materially different in the future. In addition, if our actual forfeiture rate is materially different from our estimate, the stock-based

compensation expense could be significantly different from what we have recorded in the current period.

Impairment of Long-lived Assets

We assess impairment of long-lived assets, which include property and equipment, on at least an annual basis and when events or changes in circumstances indicate that their carrying amount may not be recoverable. Circumstances which could trigger a review include, but are not limited to, significant decreases in the market price of the asset, significant adverse changes in the business climate or legal factors, accumulation of costs significantly in excess of the amount originally expected for the acquisition or construction of the asset, current period cash flow or operating losses combined with a history of losses or a forecast of continuing losses associated with the use of the asset, or expectations that the asset will more likely than not be sold or disposed of significantly before the end of its estimated useful life. To date we have not recorded any impairment charges.

Inventories

Inventory is valued at the lower of standard cost, which approximates actual cost, or market. Cost is determined using the FIFO (first-in, first-out) method. Adjustments to reduce the cost of inventory to its net realizable value, if required, are made for estimated excess or obsolete balances.

We enter into inventory purchases and commitments so that we can meet future shipment schedules based on forecasted demand for our products. The business environment in which we operate is subject to rapid changes in technology and customer demand. We perform a detailed assessment of inventory each period, which includes a review of, among other factors, demand requirements, product life cycle and development plans, component cost trends, product pricing, product expiration, and quality issues. Based on our analysis, we record adjustments to inventory for potentially excess, obsolete, or impaired goods, when appropriate, in order to report inventory at net realizable value. Inventory adjustments may be required if actual demand, component costs, supplier arrangements, or product life cycles differ from our estimates. Any such adjustments would result in a charge to our results of operations.

Leases

We categorize leases at their inception as either operating or capital leases. On certain of our lease agreements, we received tenant improvement allowances, rent holidays and/or other incentives. Rent expense is recorded on a straight-line basis over the term of the lease. The difference between rent expense accrued and amounts paid under the lease agreement is recorded as deferred rent in the accompanying balance sheets. Leasehold improvements are capitalized at cost and depreciated over the shorter of their expected useful life or the life of the lease. To the extent leasehold improvement allowances are afforded to us by the landlord, we record the tenant improvements as leasehold improvement assets with a corresponding deferred rent liability. We establish assets and liabilities for the construction costs incurred under build-to-suit lease arrangements to the extent we are involved in the construction of structural improvements or take some level of financial or construction risk prior to commencement of a lease.

For build-to-suit lease arrangements, we evaluate the extent of our financial and operational involvement in the tenant improvements to determine whether we are considered the owner of the construction project under GAAP. When we are considered the owner of a project, we record the shell of the facility at its fair value at the date construction commences with a corresponding facility financing obligation. Improvements to the facility during the construction project are capitalized and, to the extent funded by lessor afforded incentives, with corresponding increases to the facility financing obligation. Payments we make under leases in which we are considered the owner of the facility are allocated to land rental expense, based on the relative values of the land and building at the commencement of construction, reductions of the facility financing obligation and interest expense recognized on the outstanding obligation. To the extent gross future payments do not equal the recorded liability, the liability is settled upon return of the facility to the lessor. Any difference between the book value of the assets and remaining facility obligation are recorded in other income (expense), net. For existing arrangements, the differences are expected to be immaterial.

Income Taxes

We are subject to income taxes in the United States and certain states in which we operate, and we use estimates in determining our provisions for income taxes. Significant management judgment is required in determining our provision for income taxes, deferred tax assets and liabilities and valuation allowances recorded against net deferred tax assets in accordance with U.S. GAAP. These estimates and judgments occur in the calculation of tax credits, benefits, and deductions, and in the calculation of certain tax assets and liabilities, which arise from differences in the timing of recognition of revenue and expense for tax and financial statement purposes, as well as the interest and penalties related to uncertain tax positions. Significant changes to these estimates may result in an increase or decrease to our tax provision in the current or subsequent period.

At December 31, 2014, we maintained a full valuation allowance against all of our deferred tax assets which totaled \$275.0 million, including net operating loss carryforwards and research and development tax credits of \$225.1 million and \$24.9 million, respectively. Our deferred tax assets include federal and state net operating loss carryforwards of approximately \$579.7 million and \$526.6 million, respectively, and federal and state research and development credit carryforwards of approximately \$21.0 million and \$22.3 million, respectively. The federal net operating loss carryforward begins expiring in 2024, the state net operating loss carryforward have begun expiring in 2014 and the federal research and development credits begin expiring in 2024. The California tax research and development credits can be carried forward indefinitely.

We assess all material positions taken in any income tax return, including all significant uncertain positions, in all tax years that are still subject to assessment or challenge by relevant taxing authorities. Assessing an uncertain tax position begins with the initial determination of the position's sustainability and is measured at the largest amount of benefit that is greater than 50% likely of being realized upon ultimate settlement. As of each balance sheet date, unresolved uncertain tax positions must be reassessed, and we will determine whether the factors underlying the sustainability assertion have changed and the amount of the recognized tax benefit is still appropriate.

Recent Accounting Pronouncements

In May 2014, the Financial Accounting Standards Board ("FASB") issued Accounting Standards Update ("ASU") 2014-09, Revenue from Contracts with Customers, requiring entities to recognize revenue to which they expect to be entitled to for the transfer of promised goods or services to customers. The updated standard will replace most existing revenue recognition guidance in U.S. GAAP when it becomes effective and permits the use of either a retrospective or cumulative effect transition method. The updated standard is effective for us beginning in the first quarter of fiscal year 2017 and early adoption is not permitted. We are evaluating the impact of adopting this ASU on our financial statements and related disclosures.

In August 2014, the FASB issued ASU No. 2014-15, Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern. This ASU introduces an explicit requirement for management to assess if there is substantial doubt about an entity's ability to continue as a going concern, and to provide related footnote disclosures in certain circumstances. Disclosures are required if conditions give rise to substantial doubt. This ASU is effective for us for the year ending December 31, 2016.

Results of Operations

Comparison of the Years Ended December 31, 2014 and 2013

	Year Ended December 31,			
	2014	2013	\$ Change	% Change
Revenue:	(in thousands, except percentages)			
Product revenue	\$ 35,299	\$ 20,039	\$ 15,260	76%
Service and other revenue	8,511	6,446	2,065	32%
Contractual revenue	16,784	1,696	15,088	890%
Total revenue	60,594	28,181	32,413	115%
Cost of Revenue:				
Cost of product revenue	29,626	15,706	13,920	89%
Cost of service and other revenue	7,566	6,056	1,510	25%
Total cost of revenue	37,192	21,762	15,430	71%
Gross profit	23,402	6,419	16,983	265%
Operating Expense:				
Research and development	48,230	45,217	3,013	7%
Sales, general and administrative	38,026	38,745	(719)	(2%)
Total operating expense	86,256	83,962	2,294	3%
Operating loss	(62,854)	(77,543)	14,689	19%
Interest expense	(2,828)	(2,478)	(350)	(14%)
Other income (expense), net	(478)	728	(1,206)	(166%)
Net loss	\$ (66,160)	\$ (79,293)	\$ 13,133	17%

Revenue

Revenue for the year ended December 31, 2014 totaled \$60.6 million compared to \$28.2 million for the year ended December 31, 2013. The revenue increased in all categories, including sales of instruments, consumables, service and other revenue, and contract revenue from the Roche Agreement.

	Year Ended		\$ Change	% Change
	2014	2013		
Revenue:	(in thousands, except percentages)			
Instrument revenue	\$ 22,125	\$ 11,521	\$ 10,604	92%
Consumable revenue	13,174	8,518	4,656	55%
Total product revenue	35,299	20,039	15,260	76%
Service and other revenue	8,511	6,446	2,065	32%
Contractual revenue	16,784	1,696	15,088	890%
Total revenue	\$ 60,594	\$ 28,181	32,413	115%

Product revenue for the year ended December 31, 2014 consisted of \$22.1 million from sales of our instruments and instrument upgrades and \$13.2 million from sales of consumables, compared to \$11.5 million from sales of our instruments and \$8.5 million from sales of consumables in the year ended December 31, 2013. Instrument revenue for the years ended December 31, 2014 and 2013 reflects revenue derived from the delivery of 38 and 17 instruments during the periods, respectively. The increase in consumable sales reflects our larger installed instrument base and higher sales of consumables per instrument within the installed base.

Service and other revenue for the year ended December 31, 2014 primarily consisted of service revenue of \$8.4 million compared to service revenue of \$6.1 million for the year ended December 31, 2013. Service revenue was, and continues to be, derived from product maintenance agreements sold on our installed instruments. The increase in service revenue was primarily attributable to a larger installed instrument base in 2014.

Contractual revenue for the year ended December 31, 2014 consists of a full year of quarterly amortization of \$1.7 million and our achievement of a development milestone for which we received a \$10.0 million payment from Roche. During 2013, contractual revenue included \$1.7 million, representing one quarter of amortization. As of December 31, 2014, \$26.5 million remained deferred and will be amortized as revenue over the remaining estimated obligation period. The amortization period is based upon management's expectations of delivering pursuant to the Roche Agreement and is subject to change based on multiple factors including progress towards deliverables under the contract.

Gross Profit

Gross profit for the year ended December 31, 2014 totaled \$23.4 million, resulting in a gross margin of 38.6%, compared to a \$6.4 million gross profit for the year ended December 31, 2013 and a gross margin of 22.8%. The increase for both gross margin and gross profit is primarily due to the increase in contractual revenue, specifically the \$10.0 million relating to the achievement of a development milestone and an increase in contractual revenue amortization of \$5.1 million during 2014.

Cost of product revenue of \$29.6 million for the year ended December 31, 2014 reflects the costs primarily relating to the sale of 38 instruments and consumables shipped during the period while cost of product revenue of \$15.7 million for the year ended December 31, 2013 reflects the costs primarily relating to the sale of 17 instruments and consumables shipped during the period. The increase of \$13.9 million in cost of product revenue for the year ended December 31, 2014 compared to the year ended December 31, 2013 was primarily due to the higher quantity of instruments and consumables shipped during the year ended December 31, 2014.

Cost of service and other revenue for the year ended December 31, 2014 increased to \$7.6 million compared to \$6.1 million for the year ended December 31, 2013. The increase in cost of service and other revenue reflected higher service costs for personnel, materials and support infrastructure necessary to support the rising installed base of our instruments.

Gross margin for 2015 is expected to remain variable depending on the revenue mix, including in particular, the amount of contractual revenue.

Research and Development Expense

Research and development expense consists primarily of expenses for personnel engaged in the development of our SMRT technology, the design and development of our future products and current product enhancements. These expenses also include prototype-related expenditures, development equipment and supplies, facilities costs and other related overhead. We expense research and development costs during the period in which the costs are incurred. However, we defer and capitalize non-refundable advance payments made for research and development activities until the related goods are received or the related services are rendered.

For the year ended December 31, 2014, research and development expenses increased \$3.0 million, or 7%, compared to the year ended December 31, 2013. The increase in research and development expense was primarily attributed to an increase of \$2.4 million in personnel-related expense and higher external product development expenses. Research and development expense includes stock-based compensation of \$3.8 million and \$4.1 million during the years ended December 31, 2014 and 2013, respectively. We expect our research and development expenses to increase in 2015.

Sales, General and Administrative Expense

Selling, general and administrative expenses include costs for sales, marketing and administrative personnel, sales and marketing activities, tradeshow expenses, legal expenses, regulatory fees and general corporate expenses.

Selling, general and administrative expenses for the year ended December 31, 2014 remained relatively flat compared to the year ended December 31, 2013. Selling, general and administrative expenses include stock-based compensation of \$5.4 million and \$5.3 million during the years ended December 31, 2014 and 2013, respectively. We expect our selling, general and administrative expenses to increase in 2015.

Interest Expense

Interest expense for the year ended December 31, 2014 remained relatively flat compared to the year ended December 31, 2013. Interest expense was related primarily to the debt facility entered into during the year ended December 31, 2013.

Other Income (Expense), Net

Other income (expense), net consists primarily of interest income earned on cash and investments, accretion of discounts and amortization of premiums related to investments, net gains or losses on foreign currency transactions, net gains or losses resulting from changes in the estimated fair value of the financing derivative and foreign income taxes.

Comparison of the Years Ended December 31, 2013 and 2012

	Year Ended December 31,			
	2013	2012	\$ Change	% Change
	(in thousands, except percentages)			
Revenue:				
Product revenue	\$ 20,039	\$ 20,089	\$ (50)	0%
Service and other revenue	6,446	5,894	552	9%
Contractual revenue	1,696	—	1,696	—
Total revenue	28,181	25,983	2,198	8%
Cost of Revenue:				
Cost of product revenue	15,706	18,796	(3,090)	(16%)
Cost of service and other revenue	6,056	6,247	(191)	(3%)
Total cost of revenue	21,762	25,043	(3,281)	(13%)
Gross profit	6,419	940	5,479	583%
Operating Expense:				
Research and development	45,217	47,623	(2,406)	(5%)
Sales, general and administrative	38,745	47,655	(8,910)	(19%)
Total operating expense	83,962	95,278	(11,316)	(12%)
Operating loss	(77,543)	(94,338)	16,795	18%
Interest expense	(2,478)	(274)	(2,204)	(804%)
Other income, net	728	147	581	395%
Net loss	\$ (79,293)	\$ (94,465)	\$ 15,172	16%

Revenue

Revenue for the year ended December 31, 2013 totaled \$ 28.2 million compared to \$26.0 million for the year ended December 31, 2012.

Product revenue in the year ended December 31, 2013 consisted of \$11.5 million from sales of our instruments and instrument upgrades and \$8.5 million from sales of consumables compared to \$15.5 million from sales of our instruments and \$4.6 million from sales of consumables in the year ended December 31, 2012. Instrument revenue for the years ended December 31, 2013 and 2012 reflects revenue from 17 and 23 instruments during the periods, respectively. The increase in consumable sales is primarily attributable to a larger installed instrument base and higher utilization.

Service and other revenue during the year ended December 31, 2013 primarily consisted of service revenue of \$6.1 million and grant revenue of \$0.3 million compared to service revenue of \$5.0 million and grant revenue of \$0.9 million for the year ended December 31, 2012. Service revenue was derived from product maintenance agreements sold on our installed instruments and the increase in service revenue from 2012 to 2013 was primarily attributable to a larger installed instrument base in 2013. Grant revenue represents amounts earned under research agreements with government entities which are recognized in the period during which the related costs are incurred.

Contractual revenue was \$1.7 million for the year ended December 31, 2013. Under the Roche Agreement, we received a non-refundable up-front payment of \$35.0 million, of which \$1.7 million was recognized as revenue for the year ended December 31, 2013 and the remaining \$33.3 million is deferred and will be amortized as revenue over the estimated obligation periods with \$6.8 million expected to be recognized as revenue during 2014.

Gross Profit

Gross profit for the year ended December 31, 2013 totaled \$6.4 million, resulting in a gross margin of 22.8%, compared to a \$0.9 million gross profit for the year ended December 31, 2012 and a gross margin of 3.6%. The \$5.5 million increase in gross profit from 2012 to 2013 primarily resulted from an increase in higher margin consumable sales, lower product and service costs, and \$1.7 million of gross profit recognized in 2013 in relation to the Roche Agreement. Cost of revenue for the year ended December 31, 2012 included \$0.7 million of expense associated with a new product release in the first quarter of 2012 and a \$0.9 million charge associated with a provision for excess and obsolete inventory based on a review of on hand inventory and future demand. Cost of product revenue of \$15.7 million for the year ended December 31, 2013 reflected the costs relating to 17 instruments and consumables recognized in revenue during the year ended December 31, 2013, compared with \$18.8 million for the year ended December 31, 2012 reflecting the costs relating to components and manufacturing overhead incurred on the 23 instruments that were installed and consumables that were shipped during the year ended December 31, 2012.

Research and Development Expense

During the year ended December 31, 2013, research and development expenses decreased \$2.4 million, or 5%, compared to the year ended December 31, 2012. The decrease was driven primarily by a decrease of \$1.1 million in facility costs, a decrease of \$1.0 million in personnel related expense including stock-based compensation and a decrease of \$0.7 million in depreciation, partially offset by an increase of \$0.4 million in other net expenses.

Research and development expense included stock-based compensation expense of \$4.1 million and \$4.6 million during the years ended December 31, 2013 and 2012, respectively.

Sales, General and Administrative Expense

For the year ended December 31, 2013, selling, general and administrative expenses decreased \$8.9 million, or 19%, compared to the year ended December 31, 2012. The decrease was driven primarily by a decrease of \$4.6 million in legal, professional and consulting expenses primarily as a result of decreased class action litigation related expenses and other legal expenses, a decrease of \$2.3 million in marketing and travel related costs due partly to lower expenses incurred for trade show and conference expenses, a decrease of \$0.7 million in personnel related expense including stock-based compensation and a net decrease of \$1.3 million in other expenses. Sales, general and administrative expense included stock-based compensation expense of \$5.3 million and \$4.6 million during the years ended December 31, 2013 and 2012, respectively.

Interest Expense

Interest expense increased \$2.2 million from \$0.3 million in the year ended December 31, 2012 to \$2.5 million in the year ended December 31, 2013, primarily as a result of a debt facility entered into during the first quarter of 2013.

Liquidity and Capital Resources

Liquidity

Since our inception we have financed our operations primarily through the issuance of common and preferred stock.

Cash and investments at December 31, 2014 totaled \$101.3 million, compared to \$112.5 million at December 31, 2013. For the year ended December 31, 2014, we received \$38.0 million, net, through the sale of common stock under our “at-the-market” offering. Excluding proceeds from the “at-the-market” offering of \$38.0 million, cash and investments decreased by \$49.2 million compared to December 31, 2013, primarily reflecting \$51.5 million of cash used in operating activities and \$1.6 million of fixed asset purchases, partially offset by \$4.0 million of proceeds received from equity sales through our employee equity plans.

We believe that existing cash, cash equivalents and investments will be sufficient to fund our projected operating requirements for at least 12 months; however, we plan to raise additional capital in the future. These expectations are based on our current operating and financing plans, which are subject to change. Factors that may affect our capital needs include, but are not limited to, slower than expected adoption of our products resulting in lower sales of our

products and services; future acquisitions; our ability to maintain new collaboration and customer arrangements; the progress of our research and development programs; initiation or expansion of research programs and collaborations; the costs involved in preparing, filing, prosecuting, defending and enforcing intellectual property rights; the purchase of patent licenses; and other factors.

To the extent 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. There can be no assurance that such funds will be available on favorable terms, or at all. If adequate funds are not available, we may be required to curtail operations significantly or to obtain funds by entering into collaboration agreements on unattractive terms. Our inability to raise capital could have a material adverse effect on our business, financial condition and results of operations.

The following table summarizes our cash flows activities for the periods indicated.

	Year Ended December 31,		
	2014	2013	2012
	(in thousands)		
Net cash provided by (used in):			
Operating activities	\$ (51,468)	\$ (29,833)	\$ (76,822)
Investing activities	19,564	(33,117)	61,792
Financing activities	41,991	42,772	2,705

Operating Activities

Our primary uses of cash in operating activities are for the development of ongoing product enhancements and future products manufacturing and sale of PacBio RS II instruments and consumables, and support functions related to our selling, general and administrative activities. The net cash used for the years ended December 31, 2014, 2013 and 2012 primarily reflects the net loss for those periods, partially offset by non-cash operating expenses including depreciation, stock-based compensation, and changes in working capital.

Cash used in operating activities of \$51.5 million during 2014 reflected a net loss of \$66.2 million, partially offset by non-cash stock-based compensation of \$9.9 million and depreciation and amortization of \$4.2 million. The change in net operating assets and liabilities was primarily due to (i) an increase of \$3.9 million in accounts payable and (ii) an increase of \$3.5 million in accrued expenses, partially offset by \$6.8 million in deferred contractual revenue during 2014.

Cash used in operating activities of \$29.8 million during 2013 reflected a net loss of \$79.3 million, partially offset by non-cash stock-based compensation of \$9.9 million and depreciation and amortization of \$5.6 million. The change in net operating assets and liabilities was primarily due to (i) an increase of \$33.3 million of deferred development revenue associated with the Roche agreement, and (ii) the fluctuation among prepaid expenses and other assets, accounts payable, accrued expenses, and other liabilities due to the timing of payments during 2013.

Cash used in operating activities of \$76.8 million during 2012 reflected a net loss of \$94.5 million, a non-cash stock-based compensation of \$9.7 million and depreciation and amortization of \$6.6 million. Changes in working capital were due primarily to (i) inventory decreasing as a result of a decrease in the amount of instruments awaiting customer acceptance as compared to the prior year (ii) accounts receivable and deferred revenue decreasing due to the timing of instrument sales, and (iii) prepaid expenses and other assets, accounts payable, accrued expenses and other current liabilities fluctuated primarily due to the timing of vendor, litigation related, and employee compensation payments during 2012.

Investing Activities

Our investing activities consist primarily of capital expenditures and investment purchases and maturities.

In 2014, net cash provided by investing activities was \$19.6 million, comprised of net maturities of investments of \$21.2 million, partially offset by purchases of property and equipment of \$1.6 million.

In 2013, net cash used in investing activities was \$33.1 million, comprised of net purchases of investments of \$32.2 million and \$0.9 million of purchases of property and equipment.

In 2012, net cash provided by investing activities was \$61.8 million, comprised of net sales and maturities of investments of \$63.5 million, partially offset by \$1.7 million of purchases of property and equipment.

Financing Activities

In 2014, cash provided by financing activities was \$42.0 million, resulting from net proceeds of \$38.0 million from sales of our common stock using our “at-the-market” offering and \$4.0 million from the issuance of common stock through our equity compensation plans.

In 2013, cash provided by financing activities was \$42.8 million, comprised of net proceeds of \$19.8 million from our debt facility, net proceeds of \$19.9 million from our common stock “at-the-market” offering, and \$3.1 million from the issuance of our common stock through the sale of shares under our ESPP and stock option exercises.

In 2012, cash provided by financing activities was \$2.7 million, resulting from the issuance of our common stock through the sale of shares under our ESPP and stock option exercises.

Capital Resources

In November 2014, we filed a shelf registration statement on Form S-3 with the SEC pursuant to which we may, from time to time, sell up to an aggregate of \$150 million of our common stock, preferred stock, depositary shares, warrants, units or debt securities. On November 21, 2014, the registration statement was declared effective by the SEC, which will allow us to access the capital markets for the three-year period following the effective date.

Debt facility and warrant agreement

Under the terms of our February 2013 debt agreement with Deerfield (the "Facility Agreement"), we received \$20.5 million and we issued promissory notes in the aggregate principal amount of \$20.5 million (the "Notes"). The Notes bear simple interest at a rate of 8.75% per annum, payable quarterly in arrears commencing on April 1, 2013 and on the first business day of each January, April, July and October thereafter. We received net proceeds of \$20.0 million, representing \$20.5 million of gross proceeds, less a \$500,000 facility fee, before deducting other expenses of the transaction.

The Facility Agreement also contains various representations and warranties, and affirmative and negative covenants, customary for financings of this type, including restrictions on our ability to incur additional indebtedness or liens on our assets, except as permitted under the Facility Agreement. In addition, we are required to maintain consolidated cash and cash equivalents on the last day of each calendar quarter of not less than \$2.0 million. As security for our repayment of our obligations under the Facility Agreement, we granted a security interest in substantially all of our property and interests in property.

Common stock "at-the-market" offering

On October 5, 2012, we entered into a sales agreement pursuant to which we may offer and sell, from time to time, shares of our common stock having an aggregate offering price of up to \$30.0 million through an "at-the-market" offering. On November 8, 2013, the sales agreement was amended to increase the shares of our common stock that may be sold pursuant to the sales agreement by an additional aggregate offering price of \$30.0 million. On February 3, 2015, the sales agreement was amended again in order to increase the shares of our common stock that may be sold pursuant to the sales agreement by an additional aggregate offering price of \$30.0 million. We pay a commission equal to 3% of the gross proceeds from the sale of shares of our common stock under the sales agreement. We intend to use the net proceeds from this offering for general corporate purposes, including capital expenditures and working capital. 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. We are not obligated to make any sales of shares of our common stock under the sales agreement. As of December 31, 2014, we have sold a total of 14.1 million shares of our common stock at an average price of \$4.27 through our "at-the-market" offering, for total net proceeds of \$58.0 million.

At the election of the holders representing a majority of the aggregate principal amount of the outstanding Notes issued pursuant to the Facility Agreement, the holders may elect to receive 25% of the net proceeds from any financing that includes an equity component, including without limitation, sales pursuant to our "at-the-market" offering. This right is subject to certain exceptions set forth in the Facility Agreement, including that the right will not apply until we have issued 15.0 million shares of our common stock following the date of the Facility Agreement. To the extent we raise additional capital in the future through the sale of common stock under our "at the market" offering,

we may be obligated, at the election of the holders of the Notes, to pay 25% of the net proceeds from any such financing activities as payment of the Notes.

Contractual Obligations, Commitments and Contingencies

The following table provides summary information concerning our future contractual obligations as of December 31, 2014.

	Payments due by period (in thousands)			
	Total	less than 1 year	1-3 years	More than 3 years
Purchase commitments and obligations	\$ 13,648	\$ 13,648	\$ —	\$ —
Operating lease obligations (1)	4,079	3,984	95	—
Facility financing obligation	668	668	—	—
Debt (2)	28,978	1,794	9,225	17,959
Total contractual obligations	\$ 47,373	\$ 20,094	\$ 9,320	\$ 17,959

(1) Maintenance, insurance, taxes and contingent rent obligations are excluded. Our current lease obligations for our headquarters in Menlo Park expire at the end of 2015. See “Note 8. Commitments and Contingencies” in Part II, Item 8 of this Form 10-K for additional information.

(2) Under the terms of the Debt, we received \$20.5 million in funding. The amounts in the table above include interest and principal repayments on the debt. Please see “Note 6. Notes payable” in Part II, Item 8 of this Form 10-K for additional information.

Purchase commitments and obligations

These amounts include an estimate of all open purchase orders and contractual obligations in the ordinary course of business, including commitments with contract manufacturers and suppliers, for which we have not received the goods or services. A majority of these purchase obligations are due within a year. Although open purchase orders are considered enforceable and legally binding, the terms generally allow us the option to cancel, reschedule, and adjust our requirements based on our business needs prior to the delivery of goods or performance of services.

Facility Financing Obligation

In December 2009 we entered into a build-to-suit lease agreement for a manufacturing and office facility where we are considered the owner of the project under GAAP. When we are considered the owner of a project, we record the shell of the facility at its fair value at the date construction commences with a corresponding facility financing obligation. Accordingly, we recorded \$3.0 million of building and leasehold improvement assets and a corresponding liability to facility financing obligation.

The table above reflects only payment obligations that are fixed and determinable. Milestone payments and royalty payments under our license agreements are not included in the table above because we cannot, at this time, determine when or if the events triggering the commencement of payment obligations will become potentially payable.

License Agreements

Payments related to licensing and other arrangements not included in the contractual obligations table include amounts related to cancelable license agreements with third parties for certain patent rights and technology. Under the terms of these agreements, we may be obligated to pay royalties based on revenue from the sales of licensed products, or minimum royalties, whichever is greater, and license maintenance fees. The future license maintenance fees and minimum royalty payments under the license agreements are not deemed to be material.

Off-Balance Sheet Arrangements

As of December 31, 2014 we did not have any off-balance sheet arrangements.

In the ordinary course of business, we enter into standard indemnification arrangements. Pursuant to these arrangements, we indemnify, hold harmless, and agree to reimburse the indemnified parties for losses suffered or incurred by the indemnified party in connection with any trade secret, copyright, patent or other intellectual property infringement claim by any third party with respect to its technology, or from claims relating to our performance or non-performance under a contract, any defective products supplied by us, or any negligent acts or omissions, or willful misconduct, committed by us or any of our employees, agents or representatives. The term of these indemnification agreements is generally perpetual after the execution of the agreement. The maximum potential amount of future payments we could be required to make under these agreements is not determinable because it involves claims that may be made against us in future periods, but have not yet been made. To date, we have not incurred costs to defend lawsuits or settle claims related to these indemnification agreements.

We also enter and have entered into indemnification agreements with our directors and officers that may require us to indemnify them against liabilities that arise by reason of their status or service as directors or officers, except as

prohibited by applicable law. In addition, we may have obligations to hold harmless and indemnify third parties involved with our fund raising efforts and their respective affiliates, directors, officers, employees, agents or other representatives against any and all losses, claims, damages and liabilities related to claims arising against such parties pursuant to the terms of agreements entered into between such third parties and us in connection with such fund raising efforts. To the extent that such indemnification obligations apply to the lawsuits described in “Note 8.

Commitments and Contingencies” in Part II, Item 8 of this Form 10-K, any associated expenses incurred are included within the related accrued litigation expense amounts. No additional liability associated with such indemnification agreements has been recorded at December 31, 2014.

ITEM 7A. Quantitative and Qualitative Disclosures About Market Risk

Interest Rate and Market Risk

Our exposure to market risk is confined to our cash, cash equivalents and our investments. The goals of our investment policy are preservation of capital, fulfillment of liquidity needs and fiduciary control of cash and cash equivalents and investments. We also seek to maximize income from our investments without assuming significant risk. To achieve our goals, we maintain a portfolio of cash equivalents and investments in a variety of securities of high credit quality. The securities in our investment portfolio are not leveraged, are classified as available for sale and are, due to their short-term nature, subject to minimal interest rate risk. We currently do not hedge interest rate exposure. Because of the short-term maturities of our investments, we do not believe that an increase in market rates would have any material negative impact on the value of our investment portfolio.

Foreign Exchange Risk

The majority of our revenue, expense, and capital purchasing activities are transacted in U.S. dollars. However, a portion of our operations consists of development and sales activities outside of the United States, therefore we have foreign exchange exposures relating to non-U.S. dollar revenue, operating expense, accounts receivable, accounts payable and currency balances. Our primary exposure is with the Euro. A 10% strengthening of the U.S. dollar exchange rate against all currencies with which we have exposure, after taking into account offsetting positions at December 31, 2014 would have resulted in a \$0.6 million decrease in the carrying amounts of those net assets. Actual gains and losses in the future may differ materially from the hypothetical gains and losses discussed above based on changes in the timing and amount of foreign currency exchange rate movements and our actual exposure.

Our international operations are subject to risks typical of international operations, including, but not limited to, differing economic conditions, changes in political climate, differing tax structures, other regulations and restrictions and foreign exchange rate volatility.

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ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTAL DATA

PACIFIC BIOSCIENCES OF CALIFORNIA, INC.

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REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

The Board of Directors and Stockholders of Pacific Biosciences of California, Inc.

We have audited the accompanying consolidated balance sheets of Pacific Biosciences of California, Inc. as of December 31, 2014 and 2013, and the related consolidated statements of operations and comprehensive loss, stockholders' equity, and cash flows for each of the three years in the period ended December 31, 2014. Our audits also included the financial statement schedule listed in the Index at Item 15(a). These financial statements and schedule are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements and schedule based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the consolidated financial position of Pacific Biosciences of California, Inc. at December 31, 2014 and 2013, and the consolidated results of its operations and its cash flows for each of the three years in the period ended December 31, 2014, in conformity with U.S. generally accepted accounting principles. Also, in our opinion, the related financial statement schedule, when considered in relation to the basic financial statements taken as a whole, presents fairly in all material respects the information set forth therein.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), Pacific Biosciences of California, Inc.'s internal control over financial reporting as of December 31, 2014, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework), and our report dated March 12, 2015 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

Redwood City, California

March 12, 2015

PACIFIC BIOSCIENCES OF CALIFORNIA, INC.

Consolidated Balance Sheets

(in thousands, except per share amounts)	December 31,	
	2014	2013
Assets		
Current assets		
Cash and cash equivalents	\$ 36,449	\$ 26,362
Investments	64,899	86,166
Accounts receivable	3,406	2,746
Inventory, net	11,335	10,050
Prepaid expenses and other current assets	1,671	1,135
Total current assets	117,760	126,459
Property and equipment, net	6,601	9,236
Other long-term assets	162	490
Total assets	\$ 124,523	\$ 136,185
Liabilities and Stockholders' Equity		
Current liabilities		
Accounts payable	\$ 5,608	\$ 1,717
Accrued expenses	11,441	7,905
Deferred service revenue, current	6,121	4,046
Deferred contractual revenue, current	6,785	6,785
Other liabilities, current	1,534	2,102
Total current liabilities	31,489	22,555
Deferred service revenue, non-current	1,129	518
Deferred contractual revenue, non-current	19,735	26,519
Other liabilities, non-current	2,153	3,517
Notes payable	14,124	13,347
Financing derivative	944	549
Total liabilities	69,574	67,005
Commitments and contingencies (Note 8)		
Stockholders' equity		
Preferred Stock, \$0.001 par value:		
Authorized 50,000 shares; No shares issued or outstanding	—	—
Common Stock, \$0.001 par value:		
Authorized 1,000,000 shares; Issued and outstanding 73,927 and 66,275 shares at December 31, 2014 and 2013, respectively	74	66
Additional paid-in-capital	736,339	684,413
Accumulated other comprehensive income	9	14
Accumulated deficit	(681,473)	(615,313)

Total stockholders' equity	54,949	69,180
Total liabilities and stockholders' equity	\$ 124,523	\$ 136,185

See accompanying notes to the consolidated financial statements.

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PACIFIC BIOSCIENCES OF CALIFORNIA, INC.

Consolidated Statements of Operations and Comprehensive Loss

(in thousands, except per share amounts)	Years ended December 31,		
	2014	2013	2012
Revenue:			
Product revenue	\$ 35,299	\$ 20,039	\$ 20,089
Service and other revenue	8,511	6,446	5,894
Contractual revenue	16,784	1,696	—
Total revenue	60,594	28,181	25,983
Cost of Revenue:			
Cost of product revenue	29,626	15,706	18,796
Cost of service and other revenue	7,566	6,056	6,247
Total cost of revenue	37,192	21,762	25,043
Gross profit	23,402	6,419	940
Operating Expense:			
Research and development	48,230	45,217	47,623
Sales, general and administrative	38,026	38,745	47,655
Total operating expense	86,256	83,962	95,278
Operating loss	(62,854)	(77,543)	(94,338)
Interest expense	(2,828)	(2,478)	(274)
Other income (expense), net	(478)	728	147
Net loss	(66,160)	(79,293)	(94,465)
Other comprehensive loss:			
Unrealized loss on investments	(5)	(16)	(27)
Comprehensive loss	\$ (66,165)	\$ (79,309)	\$ (94,492)
Net loss per share:			
Basic and diluted net loss per share	\$ (0.94)	\$ (1.26)	\$ (1.69)
Shares used in computing basic and diluted net loss per share	70,475	62,784	55,733

See accompanying notes to the consolidated financial statements.

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PACIFIC BIOSCIENCES OF CALIFORNIA, INC.

Consolidated Statements of Stockholders' Equity

(in thousands)	Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount				
Balance at December 31, 2011	54,964	\$ 55	\$ 632,906	\$ 57	\$ (441,555)	\$ 191,463
Net loss	—	—	—	—	(94,465)	(94,465)
Other comprehensive loss	—	—	—	(27)	—	(27)
Issuance of common stock in conjunction with equity plans	1,206	1	2,704	—	—	2,705
Stock-based compensation expense	—	—	9,706	—	—	9,706
Balance at December 31, 2012	56,170	56	645,316	30	(536,020)	109,382
Net loss	—	—	—	—	(79,293)	(79,293)
Other comprehensive loss	—	—	—	(16)	—	(16)
Issuance of common stock in conjunction with equity plans	1,795	2	3,077	—	—	3,079
Issuance of common stock in conjunction with at-the-market equity offering, net of issuance costs	8,310	8	19,919	—	—	19,927
Issuance of warrants in conjunction with debt facility, net of issuance costs	—	—	6,196	—	—	6,196
Stock-based compensation expense	—	—	9,905	—	—	9,905
Balance at December 31, 2013	66,275	66	684,413	14	(615,313)	69,180
Net loss	—	—	—	—	(66,160)	(66,160)
Other comprehensive loss	—	—	—	(5)	—	(5)
Issuance of common stock in conjunction with equity plans	1,901	2	3,966	—	—	3,968
Issuance of common stock in conjunction with at-the-market equity offering, net of issuance costs	5,751	6	38,017	—	—	38,023
Stock-based compensation expense	—	—	9,943	—	—	9,943
Balance at December 31, 2014	73,927	\$ 74	\$ 736,339	\$ 9	\$ (681,473)	\$ 54,949

See accompanying notes to the consolidated financial statements.

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PACIFIC BIOSCIENCES OF CALIFORNIA, INC.

Consolidated Statements of Cash Flows

(in thousands)	Years Ended December 31,		
	2014	2013	2012
Cash flows from operating activities			
Net loss	\$ (66,160)	\$ (79,293)	\$ (94,465)
Adjustments to reconcile net loss to net cash used in operating activities			
Depreciation and amortization	4,221	5,648	6,649
Amortization of debt discount and financing costs	793	595	—
Stock-based compensation	9,943	9,905	9,705
Other items	507	(352)	1,295
Changes in assets and liabilities			
Accounts receivable	(660)	76	1,735
Inventory	(1,285)	(60)	4,761
Prepaid expenses and other assets	(224)	840	50
Accounts payable	3,891	(1,271)	(1,754)
Accrued expenses	3,536	1,327	(1,333)
Deferred service revenue	2,686	386	(1,674)
Deferred contractual revenue	(6,784)	33,304	—
Other liabilities	(1,932)	(938)	(1,791)
Net cash used in operating activities	(51,468)	(29,833)	(76,822)
Cash flows from investing activities			
Purchase of property and equipment	(1,609)	(909)	(1,703)
Purchase of investments	(126,413)	(201,547)	(87,889)
Sales of investments	—	100	7,896
Maturities of investments	147,586	169,239	143,488
Net cash provided by (used in) investing activities	19,564	(33,117)	61,792
Cash flows from financing activities			
Proceeds from issuance of common stock from equity plans	3,968	3,079	2,705
Proceeds from issuance of common stock from at-the-market equity offering, net of issuance costs	38,023	19,927	—
Proceeds from issuance of debt agreement, net of issuance costs	—	19,766	—
Net cash provided by financing activities	41,991	42,772	2,705
Net increase (decrease) in cash and cash equivalents	10,087	(20,178)	(12,325)
Cash and cash equivalents at beginning of period	26,362	46,540	58,865
Cash and cash equivalents at end of period	\$ 36,449	\$ 26,362	\$ 46,540
Supplemental disclosure of cash flow information			
Interest paid	\$ 1,794	\$ 1,165	\$ —

Supplemental disclosure of non-cash investing and financing activities

Inventory transferred to (from) property and equipment for internal use	—	(558)	1,164
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See accompanying notes to the consolidated financial statements.

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PACIFIC BIOSCIENCES OF CALIFORNIA, INC.

Notes to Consolidated Financial Statements

NOTE 1. OVERVIEW

Pacific Biosciences of California, Inc., (“Pacific Biosciences”, the “Company”, “we”, “us”) has commercialized the PacBio RS II High Resolution Genetic Analyzer to help scientists solve genetically complex problems. Based on our novel Single Molecule, Real-Time (SMRT®) technology, our products enable: de novo genome assembly to finish genomes in order to more fully identify, annotate and decipher genomic structures; full-length transcript analysis to improve annotations in reference genomes, characterize alternatively spliced isoforms and find novel genes; targeted sequencing to more comprehensively characterize genetic variations; and DNA base modification identification to help characterize epigenetic regulation and DNA damage. Our technology combines very high consensus accuracy and long read lengths with the ability to detect real-time kinetic information.

The names “Pacific Biosciences,” “PacBio,” “SMRT,” “SMRTbell” and our logo are our trademarks.

NOTE 2. SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

Basis of Presentation and Consolidation

Our consolidated financial statements have been prepared in conformity with accounting principles generally accepted in the United States, or GAAP, as set forth in the Financial Accounting Standards Board, or FASB, Accounting Standards Codification, or ASC. The consolidated financial statements include the accounts of Pacific Biosciences and our wholly owned subsidiaries. All intercompany transactions and balances have been eliminated. Translation adjustments resulting from translating foreign subsidiaries’ results of operations and assets and liabilities into U.S. dollars are immaterial for all periods presented.

Use of Estimates

The preparation of financial statements in conformity with GAAP requires us to make estimates and assumptions that affect the amounts reported in the Consolidated Financial Statements and accompanying Notes to the Consolidated Financial Statements. Our estimates include, but are not limited to, the valuation of inventory, revenue valuation, the valuation of financing derivative and long-term notes, the valuation and recognition of share-based compensation, the valuation of warrants, the delivery period for collaboration agreements, the useful lives assigned to long-lived assets, and the computation provisions for income taxes. Actual results could differ materially from these estimates.

Reclassifications

Certain prior period amounts, as indicated below in details, have been reclassified to conform to current period presentation. Such reclassifications did not impact our financial position, net loss and cash flow.

- In the consolidated balance sheets as of December 31, 2013, we reclassified \$1.9 million of “Accrued expenses and other current liabilities” to “Other liabilities, current”; and
- In the consolidated statements of cash flows for the years ended December 31, 2013 and 2012, we reclassified \$66,000 and \$1,008,000 from “Prepaid expenses and other assets” to the “Other items”, respectively.

Fair Value of Financial Instruments

The carrying amount of our financial assets and liabilities, including accounts receivable, prepaid expenses, other current assets, accounts payable, accrued expenses and other current liabilities, approximate fair value due to their short maturities. The carrying value of our facility financing obligation approximates fair value based on the short duration to expected settlement, currently available borrowing rates and after consideration of non-performance risk and credit risk.

The fair value hierarchy established under GAAP requires an entity to maximize the use of observable inputs and minimize the use of unobservable inputs when measuring fair value. A financial instrument’s categorization within the fair value hierarchy is based upon the lowest level input that is significant to the fair value measurement. The three levels of inputs that may be used to measure fair value are as follows:

- Level 1: quoted prices in active markets for identical assets or liabilities;

- Level 2: inputs other than Level 1 that are observable, either directly or indirectly, such as quoted prices in active markets for similar assets or liabilities, quoted prices for identical or similar assets or liabilities in markets that are not active, or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the assets or liabilities; and
- Level 3: unobservable inputs that are supported by little or no market activity and that are significant to the fair value of the assets or liabilities.

We consider an active market as one in which transactions for the asset or liability occurs with sufficient frequency and volume to provide pricing information on an ongoing basis. Conversely, we view an inactive market as one in which there are few transactions for the asset or liability, the prices are not current, or price quotations vary substantially either over time or among market makers. Where appropriate, our non-performance risk, or that of our counterparty, is considered in determining the fair values of liabilities and assets, respectively.

Our cash deposits and money market funds are classified within Level 1 of the fair value hierarchy because they are valued using bank balances or quoted market prices. Our investments are classified as Level 2 instruments based on market pricing and other observable inputs. None of our investments are classified within Level 3 of the fair value hierarchy.

Assets and liabilities measured at fair value are classified in their entirety based on the lowest level input that is significant to the fair value measurement. Our assessment of the significance of a particular input to the entire fair value measurement requires management to make judgments and consider factors specific to the asset or liability.

Assets and liabilities measured at fair value on a recurring basis

The following table sets forth the fair value of our financial assets and liabilities that were measured on a recurring basis as of December 31, 2014 and 2013, respectively (in thousands):

(in thousands)	December 31, 2014				December 31, 2013			
	Level 1	Level 2	Level 3	Total	Level 1	Level 2	Level 3	Total
Assets								
Cash and cash equivalents:								
Cash and money market funds	\$ 21,952	\$ —	\$ —	\$ 21,952	\$ 12,963	\$ —	\$ —	\$ 12,963
Commercial paper	—	14,497	—	14,497	—	13,399	—	13,399
Total cash and cash equivalents	21,952	14,497	—	36,449	12,963	13,399	—	26,362
Investments:								
Commercial paper	—	43,653	—	43,653	—	61,264	—	61,264
Corporate debt securities	—	8,173	—	8,173	—	8,629	—	8,629
Asset backed securities	—	13,073	—	13,073	—	16,273	—	16,273
Total investments	—	64,899	—	64,899	—	86,166	—	86,166

Total assets measured at fair value	\$ 21,952	\$ 79,396	\$ —	\$ 101,348	\$ 12,963	\$ 99,565	\$ —	\$ 112,528
Liabilities								
Financing derivative	\$ —	\$ —	\$ 944	\$ 944	\$ —	\$ —	\$ 549	\$ 549
Total liabilities measured at fair value	\$ —	\$ —	\$ 944	\$ 944	\$ —	\$ —	\$ 549	\$ 549

The estimated fair value of the Financing Derivative liability (as defined in Note 6. Notes payable) was determined using Level 3 inputs, or significant unobservable inputs. Changes to the estimated fair value of the Financing Derivative are recorded in “Other income (expense), net” in the consolidated statements of operations and comprehensive loss.

The following table provides the changes in the fair value of the Financial Derivative for the year ended December 31, 2014 and 2013 (in thousands), respectively.

Financing Derivative	Amount
Balance as of January 1, 2013	\$ —
Value at issuance	967
Gain on change in fair value of Financing Derivative	(418)
Balance as of December 31, 2013	549
Loss on change in fair value of Financing Derivative	395
Balance as of December 31, 2014	\$ 944

For the year ended December 31, 2014, there were no transfers between Level 1, Level 2, or Level 3 assets or liabilities reported at fair value on a recurring basis and valuation techniques did not change compared to the prior year.

Financial assets and liabilities not measured at fair value on a recurring basis

The carrying amount of our accounts receivable, prepaid expenses, other current assets, accounts payable, accrued expenses and other current liabilities approximate fair value due to their short maturities. The carrying value of our facility financing obligation approximates fair value due to the time to maturity and prevailing market rates.

We determined the fair value of the Notes (as defined in Note 6. Notes payable) from the debt facility we entered into during the first quarter of 2013 using Level 3 inputs, or significant unobservable inputs. The value of the Notes was determined by comparing the difference between the fair value of the Notes with and without the Financing Derivative by calculating the respective present values from future cash flows using a 19.5% and 20.4% weighted average market yield. Refer to Note 6. Notes payable for additional details regarding the Notes. The estimated fair value and carrying value of the Notes are as follows (in thousands):

	December 31, 2014		December 31, 2013	
	Fair Value	Carrying Value	Fair Value	Carrying Value
Long-term notes payable	\$ 14,817	\$ 14,124	\$ 14,551	\$ 13,347

Cash and cash equivalents

We consider all highly liquid investments purchased with an original maturity of three months or less to be cash equivalents.

Investments

We have designated all investments as available-for-sale and therefore, such investments are reported at fair value, with unrealized gains and losses recognized in accumulated other comprehensive income (loss) ("OCI") in stockholders' equity. The cost of marketable securities is adjusted for the amortization of premiums and discounts to expected maturity. Premium and discount amortization is included in other income, net. Realized gains and losses, as well as interest income, on available-for-sale securities are also included in other income, net. The cost of securities sold is based on the specific identification method. We include all of our available-for-sale securities in current assets.

All of our investments are subject to a periodic impairment review. We recognize an impairment charge when a decline in the fair value of our investments below the cost basis is judged to be other-than-temporary. Factors considered in determining whether a loss is temporary include the length of time and extent to which the investments fair value has been less than the cost basis, the financial condition and near-term prospects of the investee, extent of the loss related to credit of the issuer, the expected cash flows from the security, our intent to sell the security and whether or not we will be required to sell the security before the recovery of its amortized cost. During the years ended December 31, 2014, 2013 and 2012, we did not recognize any impairment charges on our investments as it is more likely than not that we will recover their amortized cost basis upon sale or maturity.

Concentration of Credit Risk

The counterparties to the agreements relating to our investment securities consist of various major corporations, financial institutions, municipalities and government agencies of high credit standing. Our accounts receivable are derived from net revenue to customers and distributors located in the United States and other countries. We perform credit evaluations of our customers' financial condition and, generally, require no collateral from our customers. We regularly review our accounts receivable including consideration of factors such as historical experience, credit quality, the age of the accounts receivable balances and current economic conditions that may affect a customer's ability to pay. We have not experienced any significant credit losses to date.

For the year ended December 31, 2014, contractual revenue from Roche accounted for more than 10% of our total revenue. For each of the years ended December 31, 2013 and 2012, no single end customer accounted for more than 10% of our total revenue. As of December 31, 2014 and 2013, 58% and 39%, respectively, of our accounts receivable were from domestic customers. As of December 31, 2014, three customers each represented more than 10% of our net accounts receivable. As of December 31, 2013, one customer represented 37% of our net accounts receivable. No other customer represented more than 10% of our net accounts receivable as of December 31, 2013.

Inventory

Inventory is valued at the lower of standard cost, which approximates actual cost, or market. Cost is determined using the FIFO (first-in, first-out) method. Adjustments to reduce the cost of inventory to its net realizable value, if required, are made for estimated excess or obsolete balances.

Property and Equipment, Net

Property and equipment are stated at cost, net of accumulated depreciation and any impairment charges. Depreciation is computed using the straight-line method over the estimated useful life of the asset, generally two to three years for computer equipment, three to five years for software, three to seven years for furniture and fixtures, three years for lab equipment and 30 years for buildings. Leasehold improvements are depreciated over the shorter of the lease term or the estimated useful life of the related asset. Major improvements are capitalized, while maintenance and repairs are expensed as incurred.

In connection with build-to-suit lease arrangements that we account for as if we own the facility, we record the facility at the fair value at the date construction commences, prior to significant renovations, plus the costs of the renovations. We determined the fair value of such facilities prior to renovation based on several factors, including an appraisal conducted by an independent licensed appraiser.

Impairment of Long-Lived Assets

We periodically review property and equipment for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset is impaired or the estimated useful lives are no longer appropriate. Fair value is estimated based on discounted future cash flows. If indicators of impairment exist and the undiscounted projected cash flows associated with such assets are less than the carrying amount of the asset, an impairment loss is recorded to write the asset down to its estimated fair values. To date, we have not recorded any impairment charges.

Revenue Recognition

Our revenue is generated primarily from the sale of products and services, and collaboration agreements. Product revenue consists of sales of our instruments and related consumables; Service and other revenue primarily consist of revenue earned from product maintenance agreements and grant revenue. Contractual revenue relates to revenue recognized from the collaboration agreement under which we received an upfront fee and related revenue earned from the achievement of development milestones. Our deliverables under the arrangement includes licenses to intellectual property rights and research and development services.

We recognize revenue when persuasive evidence of an arrangement exists, delivery has occurred or services have been rendered, the price is fixed or determinable, and collectability is reasonably assured. For instances where final acceptance of the product or system is required, revenue is deferred until all acceptance criteria have been met. Revenue for product sales is generally recognized upon customer acceptance. Revenue for product maintenance agreements is recognized when earned, which is generally ratably over the service period. In order to assess whether the price is fixed or determinable, we evaluate whether refund rights exist. If refund rights exist or payment terms are

based on future performance, we defer revenue recognition until the price becomes fixed or determinable. We assess collectability based on a number of factors, including customer creditworthiness. If we determine that collection of amounts due is not reasonably assured, revenue recognition is deferred until receipt of payment.

We regularly enter into arrangements, comprised of one or more contracts, from which revenue is derived from multiple deliverables including a mix of products and or services. Revenue recognition for contracts with multiple deliverables is based on the individual units of accounting determined to exist in the contract. A delivered item is considered a separate unit of accounting when (i) the delivered item has value to the customer on a stand-alone basis; and (ii) if a general right of return exists, the delivery or performance of an undelivered item is considered probable and under our control. Items are considered to have stand-alone value when they are sold separately by any vendor or when the customer could resell the item on a stand-alone basis. Our revenue arrangements generally do not have a general right of return. When a deliverable does not meet the criteria to be considered a separate unit of accounting, we group it with other deliverables that, when combined, meet the criteria, and the appropriate allocation of arrangement consideration and revenue recognition is determined. Consideration is allocated at the inception of the contract to all deliverables based on their relative selling price. In order to determine the relative selling price of a deliverable, we apply, in order, vendor-specific objective evidence (“VSOE”); third-party evidence if VSOE is not available; and lastly our best estimate of selling price for the deliverable if neither VSOE nor third-party evidence is available.

In order to establish VSOE, we must regularly sell the product or service on a standalone basis with a substantial majority of sales priced within a relatively narrow range. If an insufficient number of standalone sales exist and VSOE cannot be determined, we then consider whether third party evidence can be used to establish selling price. Due to the lack of similar products and services sold by other companies within our industry, we have not established selling price using third-party evidence. If neither VSOE nor third party evidence of selling price exists, we determine our best estimate of selling price using a combination of prices set by our pricing committee adjusted for applicable discounts and customer orders received to date.

For our collaboration agreement, the process for determining estimates of selling prices of the identifiable deliverables involves significant judgments and estimates to be made by management. Our process considers multiple factors such as estimated headcount, annual research and development budget, estimated length of the research and development period and estimated transfer price on cost, which may vary over time, depending upon the circumstances, and are specific to each deliverable. If the estimated obligation period of one or more deliverables should change, the future amortization of the revenue would also change.

Deferred service revenue primarily represents product maintenance agreement revenue that is expected to be recognized over the related service period, generally one to three years.

Cost of Revenue

Cost of revenue reflects the direct cost of product components, third-party manufacturing services and our internal manufacturing overhead and customer service infrastructure costs incurred to produce, deliver, maintain and support our instruments, consumables, and services. There are no incremental costs associated with our contractual revenue; all product development costs are reflected in research and development expense.

Manufacturing overhead is predominantly comprised of labor costs. We determine and capitalize manufacturing overhead into inventory based on a standard cost model that approximates actual costs. Prior to achieving manufacturing volumes that correlated with our estimated normal capacity (the production levels expected to be achieved over a number of periods under normal circumstances with available resources), we based our capitalized overhead relative to our normal capacity. Prior to achieving normal capacity, excess manufacturing resources were engaged in research and development activities, including; next generation products, internal use research products, and general support activities. As such, manufacturing costs in excess of amounts reflected in inventory were expensed as a component of research and development expense. During 2014, manufacturing volumes trended towards and then approximated normal capacity, and excess manufacturing resources contributing to research and development activities declined significantly.

Service costs include the direct costs of components used in support, repair and maintenance of customer instruments as well as the cost of personnel, materials, shipping and support infrastructure necessary to support the installed customer base. Prior to the fourth quarter of 2013, the capacity of our existing service infrastructure exceeded the number of installed customer instruments. Therefore, management estimated the capacity of the existing service infrastructure and recognized the service-related cost of revenue based on the installed base. As a result, prior to the fourth quarter of 2013, total service infrastructure costs exceeded the costs associated with the support of customer instruments and such excess costs were included as a component of sales, general and administrative expense.

Research and Development

Research and development expense consists primarily of expenses for personnel engaged in the development of our SMRT technology, the design and development of our future products and current product enhancements. These expenses also include prototype-related expenditures, development equipment and supplies, facilities costs and other related overhead. We expense research and development costs during the period in which the costs are incurred. However, we defer and capitalize non-refundable advance payments made for research and development activities until the related goods are received or the related services are rendered.

Leases

We categorize leases at their inception as either operating or capital leases. On certain of our lease agreements, we may receive tenant improvement allowances, rent holidays and other incentives. Rent expense is recorded on a straight-line basis over the term of the lease. The difference between rent expense recognized and amounts paid under the lease agreement is recorded as deferred rent in the balance sheets. Leasehold improvements are capitalized at cost and depreciated over the shorter of their expected useful life or the life of the lease. Tenant improvements afforded to us by landlord incentives are recorded as leasehold improvement assets with corresponding deferred rent liabilities.

For build-to-suit lease arrangements, we evaluate the extent of our financial and operational involvement in the tenant improvements to determine whether we are considered the owner of the construction project under GAAP. When we are considered the owner of a project, we record the shell of the facility at its fair value at the date construction commences with a corresponding facility financing obligation. Improvements to the facility during the construction project are capitalized and, to the extent funded by lessor afforded incentives, with corresponding increases to the facility financing obligation. Payments we make under leases in which we are considered the owner of the facility are allocated to land rental expense, based on the relative values of the land and building at the commencement of construction, reductions of the facility financing obligation and interest expense recognized on the outstanding obligation. As the build-out was completed in 2010, the activity in 2014 consisted solely of lease payments. To the extent gross future payments do not equal the recorded liability, the liability is settled upon return of the facility to the lessor. Any difference between the book value of the assets and remaining facility obligation are recorded in other expense, net. For existing arrangements, the differences are expected to be immaterial.

Income Taxes

We account for income taxes under the asset and liability method, which requires, among other things, that deferred income taxes be provided for temporary differences between the tax basis of our assets and liabilities and the amounts reported in the financial statements. In addition, deferred tax assets are recorded for the future benefit of utilizing net operating losses and research and development credit carryforwards. A full valuation allowance is provided against our net deferred tax assets as it is more likely than not that the deferred tax assets will not be fully realized.

We review our positions taken relative to income taxes. To the extent our tax positions are more likely than not to result in the payout of additional taxes, we accrue the estimated amount of tax for such uncertain positions.

Stock-based Compensation

Stock-based compensation expense for all stock-based compensation awards is based on the grant date fair value estimated using the Black-Scholes option pricing model. We have limited historical information available to support the underlying estimates of certain assumptions required to value stock options. The expected term of options is estimated based on the simplified method. We do not have sufficient trading history to solely rely on the volatility of our own common stock for establishing expected volatility. Therefore, we based our expected volatility on the historical stock volatilities of our common stock as well as several comparable publicly listed companies over a period equal to the expected term of the options. The risk-free interest rate is based on the U.S. Treasury yield curve in effect at the time of grant for the expected term of the stock option. We estimate our forfeiture rate based on an analysis of our actual forfeitures and will continue to evaluate the adequacy of the forfeiture rate based on actual forfeiture experience, analysis of employee turnover behavior and other factors. The impact from a forfeiture rate adjustment will be recognized in full in the period of adjustment, and if the actual number of future forfeitures differs from that estimated, we may be required to record adjustments to stock-based compensation expense in future periods. We recognize compensation expense on a straight-line basis over the requisite service period. We elected to use the simplified method to calculate the beginning pool of excess tax benefits.

Other Comprehensive Income (loss)

Other comprehensive income (loss) is comprised of unrealized gains (losses) on our investment securities.

Recent Accounting Pronouncements

In May 2014, the Financial Accounting Standards Board ("FASB") issued Accounting Standards Update ("ASU") 2014-09, Revenue from Contracts with Customers, requiring entities to recognize revenue to which they expect to be entitled to for the transfer of promised goods or services to customers. The updated standard will replace most existing revenue recognition guidance in U.S. GAAP when it becomes effective and permits the use of either a retrospective or cumulative effect transition method. The updated standard is effective for us beginning in the first quarter of fiscal year 2017 and early adoption is not permitted. We are evaluating the impact of adopting this ASU on our financial statements and related disclosures.

In August 2014, the FASB issued ASU No. 2014-15, Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern. This ASU introduces an explicit requirement for management to assess if there is substantial doubt about an entity's ability to continue as a going concern, and to provide related footnote disclosures in certain circumstances. Disclosures are required if conditions give rise to substantial doubt. This ASU is effective for us for the year ending December 31, 2016.

NOTE 3. CONTRACTUAL REVENUE

During September 2013 we entered into a Development, Commercialization and License Agreement (the "Roche Agreement") with F. Hoffman-La Roche Ltd ("Roche"), pursuant to which we account for, and recognize as revenue, the up-front payment using the proportional performance method over the periods in which the delivery of elements of the agreement occurs. We recognize revenue using a straight line convention over the service periods of the deliverables as this method approximates our performance of services pursuant to the contract. Out of the \$35.0 million upfront cash payment received, \$6.8 million and \$1.7 million have been recognized as contractual revenue for the years ended December 31, 2014 and 2013, respectively, and \$26.5 million remain deferred as of December 31, 2014 and will be recognized as contractual revenue over the estimated obligation periods. The amortization period is based upon management's expectations of delivering pursuant to the Roche Agreement and is subject to change based on multiple factors including progress towards deliverables under the contract. Changes to management estimates could materially impact the amount of the upfront payment recognized into revenue during future periods.

In addition to the deliverables above, the Roche Agreement provides for additional payments totaling up to \$40.0 million upon the achievement of certain development milestones. Based on ASC Topic 605-28, Revenue Recognition — Milestone Method, we evaluate contingent milestones at inception of the agreement, and recognize consideration that is contingent upon the achievement of a

milestone in its entirety as revenue in the period in which the milestone is achieved only if the milestone is considered substantive in its entirety. Milestones are considered substantive if the consideration earned from the achievement of the milestone (i) is consistent with performance required to achieve the milestone or the increase in value to the delivered item, (ii) relates solely to past performance and (iii) is reasonable relative to all of the other deliverables and payments within the arrangement. During August 2014, we achieved the first development milestone and we recorded the related \$10.0 million as contractual revenue. Under the terms of the Roche Agreement, we may receive up to an additional \$30.0 million based on the achievement of additional development milestones in future periods.

NOTE 4. CASH AND CASH EQUIVALENTS AND INVESTMENTS

The following table summarizes our cash, cash equivalents and investments as of December 31, 2014 and December 31, 2013 (in thousands):

	As of December 31, 2014			
	Amortized Cost	Gross unrealized gains	Gross unrealized losses	Fair Value
Cash and cash equivalents:				
Cash and money market funds	\$ 21,952	\$ —	\$ —	\$ 21,952
Commercial paper	14,496	1	—	14,497
Total cash and cash equivalents	36,448	1	—	36,449
Investments:				
Commercial paper	43,648	5	—	43,653
Corporate debt securities	8,170	7	(4)	8,173
Asset backed securities	13,073	4	(4)	13,073
Total investments	64,891	16	(8)	64,899
Total cash, cash equivalents and investments	\$ 101,339	\$ 17	\$ (8)	\$ 101,348
	As of December 31, 2013			
	Amortized Cost	Gross unrealized gains	Gross unrealized losses	Fair Value
Cash and cash equivalents:				
Cash and money market funds	\$ 12,963	\$ —	\$ —	\$ 12,963
Commercial paper	13,398	1	—	13,399
Total cash and cash equivalents	26,361	1	—	26,362
Investments:				
Commercial paper	61,252	13	(1)	61,264
Corporate debt securities	8,620	12	(3)	8,629
Asset backed securities	16,281	2	(10)	16,273
Total investments	86,153	27	(14)	86,166

Total cash, cash equivalents and investments \$ 112,514 \$ 28 \$ (14) \$ 112,528

The following table summarizes the contractual maturities of our cash equivalents and available-for-sale investments, excluding money market funds, as of December 31, 2014:

(in thousands)	Fair Value
Due in one year or less	\$ 78,113
Due after one year through five years	1,283
Total	\$ 79,396

Actual maturities may differ from contractual maturities because issuers may have the right to call or prepay obligations without call or prepayment penalties.

NOTE 5. BALANCE SHEET COMPONENTS

Inventory:

As of December 31, 2013 and 2012, our inventory consisted of the following components:

(in thousands)	December 31,	
	2014	2013
Purchased materials	\$ 3,150	\$ 3,019
Work in process	6,115	4,012
Finished goods	2,070	3,019
Inventory	\$ 11,335	\$ 10,050

Property and Equipment, net:

As of December 31, 2014 and 2013, our property and equipment, net, consisted of the following components:

(in thousands)	December 31,	
	2014	2013
Building	\$ 1,160	\$ 1,160
Laboratory equipment and machinery	17,169	16,934
Leasehold improvements	8,348	8,111
Computer equipment	4,885	3,885
Software	4,485	4,457
Furniture and fixtures	958	926
Construction in progress	53	12
	37,058	35,485
Less: Accumulated depreciation	(30,457)	(26,249)
Property and equipment, net	\$ 6,601	\$ 9,236

Depreciation expense during the years ended December 31, 2014, 2013 and 2012 was \$4.2 million, \$5.6 million and \$6.6 million, respectively.

Accrued expenses:

As of December 31, 2014 and 2013, our accrued expenses consisted of the following:

(in thousands)	December 31,	
	2014	2013
Salaries and benefits	\$ 6,325	\$ 5,149
Accrued license and development services	3,741	1,328
Inventory accrual, professional services, accrued interest and other	1,375	1,428
Accrued expenses	\$ 11,441	\$ 7,905

NOTE 6. NOTES PAYABLE

Pursuant to a Facility Agreement (the “Facility Agreement”) we entered into with entities affiliated with Deerfield Management Company, L.P. (collectively, “Deerfield”) during February 2013, we issued promissory notes in the aggregate principal amount of \$20.5 million (the “Notes”). The Notes bear simple interest at a rate of 8.75% per annum, payable quarterly in arrears commencing on April 1, 2013. In connection with the execution of the Facility Agreement, we issued warrants to purchase an aggregate of 5,500,000 shares of common stock immediately exercisable at an exercise price per share initially equal to \$2.63 (the “Warrants”). In addition, we are required to maintain consolidated cash and cash equivalents on the last day of each calendar quarter of not less than \$2.0 million. As security for our repayment of our obligations under the Facility Agreement, we granted to Deerfield a security interest in substantially all of our property.

Financing Derivative

A number of features embedded in the Notes to the Facility Agreement required accounting for as a derivative, including the indemnification of certain withholding taxes and the acceleration of debt upon (i) a qualified financing, (ii) an Event of Default, (iii) a Major Transaction, and (iv) the exercise of the warrant via offset to debt principal. These features represent a single derivative (the “Financing Derivative”) that was bifurcated from the debt instrument and accounted for as a liability at fair value, with changes in fair value between reporting periods recorded in the other income (expense), net.

The estimated fair value of the Financing Derivative was determined by comparing the difference between the fair value of the Notes with and without the Financing Derivative by calculating the respective present values from future cash flows using a 19.5% and 20.4% weighted average market yield, respectively at December 31, 2014 and December 31, 2013, respectively. The estimated fair value of the Financing Derivative as of December 31, 2014 and December 31, 2013, was \$0.9 million and \$0.5 million, respectively.

Notes

We initially recorded the Notes and Warrants at a value of \$14.1 million and \$6.4 million, respectively, based upon the relative fair value allocation of the \$20.5 million of proceeds. The carrying value of the Notes at the inception of the debt was \$12.8 million, resulting in an original issue discount of \$7.7 million. As of December 31, 2014, \$6.4 million remains to be amortized through February 2020, the maturity of the Notes.

As of December 31, 2014, debt payments, which include interest and principal, are as follows (in thousands):

2015	\$ 1,794
2016	1,799
2017	1,794
2018	5,632
Thereafter	17,959
Total remaining payments	28,978
Less: interest and discounts	(14,854)

Notes payable \$ 14,124

NOTE 7. FACILITY FINANCING

In December 2009 we entered into a lease agreement for a manufacturing and office facility. In order for the facility to meet our needs and operating requirements, substantial tenant improvements, including improvements to the structural elements and principal operating systems of the facility, were necessary. The lessor provided a tenant improvement allowance of \$1.8 million to apply towards the necessary improvements and we remained obligated for additional amounts over the afforded allowance.

Due to our involvement in and the nature of the renovations made to the facility and our obligations to fund the costs of renovations exceeding the incentives afforded to us, we account for the facility as if we are the owner. Accordingly we recorded \$3.0 million of building and leasehold improvement assets, reflecting the \$1.2 million fair value of the facility prior to commencing renovations and the \$1.8 million of landlord incentives within property and equipment, net and a corresponding liability recorded to facility financing obligation.

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As of December 31, 2014, the future minimum payments due under the facility financing obligation were as follows:

(in thousands)	Financing obligation
2015	\$ 668
Less: interest and discounts	(416)
Total net payments under facility financing obligation	252
Property reverting to landlord	2,151
Present value of obligation	2,403
Less: current portion of obligation	(252)
Long-term portion of obligation	\$ 2,151

NOTE 8. COMMITMENTS AND CONTINGENCIES

Operating Lease Commitment

As of December 31, 2014, we have noncancelable operating lease agreements for research and development, office, manufacturing and training facilities in Menlo Park, California that expire in December 2015. Our leases have certain options to renew at rates approximating the prevailing fair market rental rate at the end of the lease term.

As of December 31, 2014, the future annual minimum lease payments under all noncancelable operating leases with remaining term in excess of one year are as follows:

Years ending December 31,	Amount (in thousands)
2015	\$ 3,984
2016	95
Total minimum lease payments	\$ 4,079

Rent expense for the years ended December 31, 2014, 2013 and 2012, was \$2.2 million, \$2.3 million and \$2.4 million, respectively. We are also required to pay our share of operating expenses with respect to the facilities in which we operate.

Other commitments include an estimated amount of approximately \$13.6 million of all open cancellable purchase orders and contractual obligations that occur in the ordinary course of business, including commitments with suppliers, for which we have not received the goods or services.

Contingencies

We become subject to claims and assessments from time to time in the ordinary course of business. We accrue liabilities for such matters when it is probable that future expenditures will be made and such expenditures can be reasonably estimated.

We may, from time to time, be party to litigation and subject to claims that arise in the ordinary course of business. In addition, third parties may, from time to time, assert claims against us in the form of letters and other communications. We currently believe that these ordinary course matters will not have a material adverse effect on our business; however, the results of litigation and claims are inherently unpredictable. Regardless of the outcome, litigation can have an adverse impact on us because of defense and settlement costs, diversion of management resources and other factors.

Indemnification

Pursuant to Delaware law and agreements entered into with each of our directors and officers, we may have obligations, under certain circumstances, to hold harmless and indemnify each of our directors and officers against losses suffered or incurred by the indemnified party in connection with their service to us, and judgments, fines, settlements and expenses related to claims arising against such directors and officers to the fullest extent permitted under Delaware law, our bylaws and certificate of incorporation. We also enter and have entered into indemnification agreements with our directors and officers that may require us to indemnify them against liabilities that arise by reason of their status or service as directors or officers, except as prohibited by applicable law. In addition, we may have obligations to hold harmless and indemnify third parties involved with our fund raising efforts and their respective affiliates, directors, officers, employees, agents or other representatives against any and all losses, claims, damages and liabilities related to claims arising against such parties pursuant to the terms of agreements entered into between such third parties and

us in connection with such fund raising efforts. To the extent that any such indemnification obligations apply to the lawsuits described above, any associated expenses incurred are included within the related accrued litigation expense amounts. No additional liability associated with such indemnification obligations has been recorded at December 31, 2014.

NOTE 9. INCOME TAXES

A reconciliation between the statutory federal income tax and our effective tax rates as a percentage of loss before income taxes are as follows:

	Years ended December 31,					
	2014		2013		2012	
Statutory tax rate	35.0	%	35.0	%	35.0	%
State tax rate, net of federal benefit	3.8		2.1		3.9	
Stock-based compensation	(1.3)		(1.7)		(1.7)	
R&D credit	4.0		4.3		1.1	
Other	(0.0)		(0.3)		(2.1)	
Change in valuation allowance	(41.5)		(39.4)		(36.2)	
Effective income tax rate	0.0	%	0.0	%	0.0	%

Temporary differences and carryforwards that gave rise to significant portions of deferred taxes are as follows (in thousands):

	December 31,	
	2014	2013
Deferred tax assets:		
Net operating loss carryforwards	\$ 225,115	\$ 214,312
Research and development credits	24,881	22,263
Depreciation	3,241	3,067
Accruals and reserves	21,737	7,390
Total deferred tax assets	274,974	247,032
Less: Valuation allowance	(273,567)	(246,186)
Deferred tax liabilities:		
Deferred rent	(1,407)	(846)
Net deferred tax assets	\$ —	\$ —

Due to uncertainties surrounding the realization of deferred tax assets through future taxable income, we have provided a full valuation allowance and, therefore, have not recognized any benefits from net operating losses and

other deferred tax assets.

Recognition of deferred tax assets is appropriate when realization of such assets is more likely than not. Based upon the weight of available evidence, we believe it is more likely than not that the net deferred tax assets will not be fully realizable. Accordingly, we have provided a full valuation allowance against our net deferred tax assets as of December 31, 2014 and 2013, respectively.

For the year ended December 31, 2014, our valuation allowance increased \$27.4 million primarily because of an increase in deferred tax assets related to net operating losses, state tax credits, and changes in accruals and reserves. For the year ended December 31, 2013, our valuation allowance increased \$31.9 million primarily because of an increase in deferred tax assets related to net operating losses, state research and development tax credits, and changes in accruals and reserves. As of December 31, 2014, we had federal and state net operating loss carryforwards of approximately \$579.7 million and \$526.6 million, respectively, available to reduce future taxable income, if any. The federal net operating loss carryforward begins expiring in 2024, and the state net operating loss carryforward began expiring in 2014.

We also had federal and California state research and development credit carryforwards of approximately \$21.0 million and \$22.3 million, respectively, as of December 31, 2014. The federal research and development credits begin expiring in 2024 if not utilized. The California tax research and development credits can be carried forward indefinitely.

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Tax attributes related to stock option windfall deductions are not recorded until they result in a reduction of cash tax payable. The tax effected benefit of the excess tax deductions of the federal and state of \$4.1 million and \$0.6 million, respectively, will be recorded to additional paid-in capital when they reduce cash tax payable.

The Tax Reform Act of 1986 limits the use of net operating loss and tax credit carryforwards in certain situations where equity transactions result in a change of ownership as defined by Internal Revenue Code Section 382. In the event we experience an additional ownership change for tax purposes, utilization of our United States net operating loss and tax credit carryforwards could be limited.

As of December 31, 2014, our total unrecognized tax benefit was \$17.0 million, of which none of the tax benefit, if recognized, would affect the effective income tax rate due to the valuation allowance that currently offsets deferred tax assets. We do not anticipate the total amount of unrecognized income tax benefits to significantly increase or decrease in the next 12 months.

A reconciliation of the beginning and ending unrecognized tax benefit accounts is as follows (in thousands):

Balance as of December 31, 2011	\$ 9,287
Increase in balance related to tax positions taken during current year	705
Balance as of December 31, 2012	9,992
Increase in balance related to tax positions taken during current year	1,642
Balance as of December 31, 2013	11,634
Increase in balance related to tax positions taken in prior year	2,959
Increase in balance related to tax positions taken during current year	2,359
Balance as of December 31, 2014	\$ 16,952

Our practice is to recognize interest and/or penalties related to income tax matters in income tax expense. As of December 31, 2014 and 2013, we had no accrued interest or penalties due to our net operating losses available to offset any tax adjustment. We file U.S. federal and various state income tax returns. For U.S. federal and state income tax purposes, the statute of limitations currently remains open for the years ending December 31, 2010 to present and December 31, 2009 to present, respectively. In addition, all of the net operating losses and research and development credit carryforwards that may be utilized in future years may be subject to examination. We are not currently under examination by income tax authorities in any jurisdiction.

NOTE 10. STOCKHOLDERS' EQUITY

Preferred Stock

Our Certificate of Incorporation, as amended and restated in October 2010 in connection with the closing of our initial public offering, authorizes us to issue 1,000,000,000 shares of \$0.001 par value common stock and 50,000,000 shares of \$0.001 par value preferred stock. As of December 31, 2014 and 2013, there were no shares of preferred stock

issued or outstanding.

Common Stock

Common stockholders are entitled to dividends when and if declared by our board of directors. There have been no dividends declared to date. The holder of each share of common stock is entitled to one vote.

During 2012, we established an at-the-market offering, pursuant to which we may offer and sell, from time to time, shares of our common stock having an aggregate offering price of up to \$30.0 million. During 2013, we established a second at-the-market offering to raise an additional \$30.0 million. We will pay a commission equal to 3% of the gross proceeds from the sale of shares of our common stock under the offering. We are not obligated to make any sales of shares of our common stock under either offering. In the year ended December 31, 2014, we issued 5.8 million shares of our common stock at an average price of \$6.81 per share through our “at-the-market” offering.

On February 3, 2015, the sales agreement was amended again to increase the aggregate offering price for shares of our common stock by an additional \$30.0 million.

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Warrants

In connection with the execution of the Facility Agreement, we issued immediately exercisable warrants to purchase 5,500,000 shares of common stock at an exercise price per share initially equal to \$2.63. The number of shares of common stock into which the warrants are exercisable and the exercise price will be adjusted to reflect any stock splits, payment of stock dividends, recapitalizations, reclassifications or other similar adjustments in the number of outstanding shares of common stock. The exercise price may also be adjusted to reflect certain dividends or other distributions, including distributions of stock or other securities, property or options by way of a dividend, spin off, reclassification, corporate rearrangement or similar transaction. As of December 31, 2014, we had outstanding exercisable warrants to purchase an aggregate of 5,500,000 shares of common stock at \$2.63 per share.

Equity Plans

As of December 31, 2014, we had three active equity plans, the 2010 Equity Incentive Plan, or “2010 Plan”, the 2010 Outside Director Equity Incentive Plan, or “2010 Director Plan”, and the 2010 Employee Stock Purchase Plan or “ESPP”, all of which we adopted upon the effectiveness of our initial public offering during October 2010. Prior to the adoption of these plans, we granted options pursuant to the 2004 Equity Incentive Plan and 2005 Stock Plan. Upon termination of the predecessor plans, the shares available for grant at the time of termination, and shares subsequently returned to the plans upon forfeiture or option termination, were transferred to the successor plan in effect at the time of share return.

We issue new shares of common stock upon exercise of stock options.

2010 Equity Incentive Plan and Outside Director Equity Incentive Plan

Stock options granted under the 2010 Plan may be either ISOs or NSOs. ISOs may be granted only to employees. NSOs may be granted to employees, consultants and directors. Stock options under the 2010 Plan may be granted with a term of up to ten years and at prices no less than the fair market value of our common stock on the date of grant. To date, stock options granted to existing employees generally vest over four years on a monthly basis and stock options granted to new employees vest at a rate of 25% upon the first anniversary of the vesting commencement date and 1/48th per month thereafter. In January 2015, an additional 3.7 million shares were reserved under the 2010 Plan.

Stock options granted under the 2010 Director Plan provide for the grant of NSOs. Stock options under the 2010 Plan may be granted with a term of up to ten years and at prices no less than the fair market value of our common stock on the date of grant. To date, stock options granted to existing directors generally vest over one year on a monthly basis and stock options granted to new directors generally vest over three years at a rate of one-third upon the first anniversary of the vesting commencement date and 1/36th per month thereafter. In January 2015, an additional 0.7 million shares were reserved under the 2010 Director Plan.

As of December 31, 2014 we reserved an aggregate of 4.9 million shares of common stock for future issuance under the 2010 Plan and 2010 Director Plan.

2010 Employee Stock Purchase Plan

We adopted the ESPP in October 2010. Our ESPP permits eligible employees to purchase common stock at a discount through payroll deductions during defined offering periods. Each offering period will generally consist of four purchase periods, each purchase period being approximately six months. The price at which the stock is purchased is equal to the lower of 85% of the fair market value of the common stock at the beginning of an offering period or at the end of a purchase period. Each offering period will generally end and the shares will be purchased twice yearly on

March 1 and September 1. As of December 31, 2014, no shares of our common stock remain available for issuance under the Plan; however the ESPP provides for an annual increase to the shares available for issuance at the beginning of each calendar year equal to 2% of the common shares then outstanding. During January 2015, an additional 1.5 million shares were reserved under the ESPP.

The following table summarizes stock option activity for all stock option plans for the year ended December 31, 2014 (in thousands, except per share amounts):

	Shares available for grant	Number of shares	Stock Options Outstanding	
			Exercise price	Weighted average exercise price
Balances, December 31, 2013	3,912	14,070	\$ 0.20 – \$ 16.00	\$ 4.81
Additional shares reserved	3,977			
Options granted	(3,505)	3,505	\$ 4.21 – \$ 7.05	\$ 6.00
Options exercised	—	(594)	\$ 0.20 – \$ 6.96	\$ 2.90
Options canceled	490	(490)	\$ 1.16 – \$ 15.98	\$ 5.90
Balances, December 31, 2014	4,874	16,491	\$ 0.70 – \$ 16.00	\$ 5.10

The following table summarizes information with respect to stock options outstanding and exercisable under the plans at December 31, 2014:

	Options Outstanding			Options Exercisable		
	Number	Weighted average remaining contractual life (Years)	Weighted average exercise price	Number vested	Weighted average exercise price	
\$ 0.00 – 1.60	1,082,067	6.78	\$ 1.11	538,693	\$ 1.04	
\$ 1.60 – 3.20	4,071,281	6.94	\$ 2.40	2,489,111	\$ 2.43	
\$ 3.20 – 4.80	4,525,775	7.53	\$ 4.08	2,296,346	\$ 4.05	
\$ 4.80 – 6.40	2,459,863	8.74	\$ 5.62	578,535	\$ 5.72	
\$ 6.40 – 8.00	1,654,881	7.68	\$ 6.99	676,966	\$ 6.99	
\$ 8.00 – 9.60	1,125,101	5.04	\$ 8.50	1,125,101	\$ 8.50	
\$ 9.60 – 11.20	354,002	5.35	\$ 10.80	353,131	\$ 10.80	
\$ 11.20 – 12.80	687,610	6.00	\$ 12.11	560,578	\$ 12.17	
\$ 12.80 – 14.40	391,334	5.99	\$ 13.87	328,010	\$ 13.83	
\$ 14.40 – 16.00	139,250	5.87	\$ 15.99	138,500	\$ 15.99	
	16,491,164	7.20	\$ 5.10	9,084,971	\$ 5.60	

The aggregate intrinsic value of the outstanding and exercisable options presented in the table above totaled \$53.3 million and \$27.6 million, respectively. The aggregate intrinsic value represents the total pretax intrinsic value (i.e., the difference between \$7.84, our closing stock price on the last trading day of our fourth quarter of 2014 and the exercise price, multiplied by the number of in-the-money options) that would have been received by the option holders had all option holders exercised their options on December 31, 2014. The amount changes based on the fair market value of our common stock. The weighted average remaining contractual life for exercisable options is 6.22 years.

The total intrinsic value of options exercised during the years ended December 31, 2014, 2013 and 2012 was \$2.0 million, \$0.5 million and \$0.7 million, respectively.

The total fair value of options vested during the years ended December 31, 2014, 2013 and 2012 was \$6.0 million, \$6.5 million and \$2.3 million, respectively.

Stock-based Compensation

Total stock-based compensation expense consists of the following (in thousands):

	Years Ended December 31,		
	2014	2013	2012
Cost of revenue	\$ 758	\$ 523	\$ 506
Research and development	3,785	4,052	4,562
Sales, general and administrative	5,400	5,330	4,637
Total stock-based compensation expense	\$ 9,943	\$ 9,905	\$ 9,705

The tax benefit of stock-based compensation expense was immaterial for the fiscal years ended December 31, 2014, 2013 and 2012.

Stock options

We estimated the fair value of employee stock option using the Black-Scholes option pricing model. The fair value of employee stock options is being amortized on a straight-line basis over the requisite service period of the awards. For the years ended December 31, 2014, 2013 and 2012, weighted average fair value at grant date for stock option was \$3.81, \$1.80 and \$1.84, respectively. We recorded stock-based compensation expense for stock options of \$7.8 million, \$7.0 million and \$6.9 million for the years ended December 31, 2014, 2013 and 2012, respectively.

For the years ended December 31, 2014, 2013 and 2012, the fair value of employee stock options was estimated using the following weighted average assumptions:

	Years Ended December 31,		
	2014	2013	2012
Expected term (years)	6.1 years	6.1 years	6.1 years
Expected volatility	70.0%	66.8%	63.4%
Risk-free interest rate	1.9%	1.3%	1.0%
Dividend yield	—	—	—

As of December 31, 2014, \$15.4 million of total unrecognized compensation expense related to stock options was expected to be recognized over a weighted-average period of 2.8 years. Future option grants will increase the amount of compensation expense to be recorded in those future periods. Cash received from option exercises for the years ended December 31, 2014, 2013 and 2012 was \$1.6 million, \$0.5 million and \$0.6 million, respectively.

ESPP

We estimated the fair value of ESPP using the Black-Scholes option pricing model. For the years ended December 31, 2014, 2013 and 2012, weighted average fair value at grant date for ESPP was \$2.98, \$1.76 and \$1.38, respectively. We recorded stock-based compensation expense for ESPP of \$2.1 million, \$2.8 million and \$2.8 million for the years ended December 31, 2014, 2013 and 2012, respectively.

For the years ended December 31, 2014, 2013 and 2012, the fair value of ESPP was estimated using the following assumptions:

	Years Ended December 31,		
	2014	2013	2012
Expected term (years)	0.5 - 2.0	0.5 - 2.0	0.5 - 2.0
Expected volatility	70.0%	70.0%	90.0%
Risk-free interest rate	0.1%-0.5%	0.1%-0.4%	0.1%-0.3%
Dividend yield	—	—	—

For the years ended December 31, 2014, 2013 and 2012, 1,325,507 shares, 1,519,366 shares and 832,878 shares of common stock were purchased under the Plan, respectively. Cash received from ESPP for the years ended December 31, 2014, 2013 and 2012 was \$2.3 million, \$2.6 million and \$2.1 million, respectively.

NOTE 11. NET LOSS PER SHARE

The following table presents the computation of basic and diluted net loss per share (in thousands, except per share amounts):

	Years Ended December 31,		
	2014	2013	2012
Numerator:			
Net loss	\$ (66,160)	\$ (79,293)	\$ (94,465)
Denominator:			
Weighted average shares used in computation of basic and diluted net loss per share	70,475	62,784	55,733
Basic and diluted net loss per share	\$ (0.94)	\$ (1.26)	\$ (1.69)

The following options outstanding and warrants to purchase common stock were excluded from the computation of diluted net loss per share for the periods presented because the effect of including such shares would have been antidilutive in the periods presented:

(in thousands)	Years Ended December 31,		
	2014	2013	2012
Options outstanding	16,491	14,070	12,016
Warrants to purchase common stock	5,500	5,500	10

NOTE 12. SEGMENT AND GEOGRAPHIC INFORMATION

We are organized as, and operate in, one reportable segment: the development, manufacturing and marketing of an integrated platform for genetic analysis. Our chief operating decision-maker is our Chief Executive Officer. The Chief Executive Officer reviews financial information presented on a consolidated basis for purposes of evaluating financial performance and allocating resources, accompanied by information about revenue by geographic regions. Our assets are primarily located in the United States of America and not allocated to any specific region and we do not measure the performance of geographic regions based upon asset-based metrics. Therefore, geographic information is presented only for revenue. Revenue by geographic region is based on the ship to address on the customer order.

A summary of our revenue by geographic location for the years ended December 31, 2014, 2013 and 2012 is as follows:

	Years Ended December 31,		
(in millions)	2014	2013	2012
United States	\$ 34.8	\$ 13.6	\$ 11.4
Europe	10.1	9.2	6.6
Asia	15.7	5.4	8.0
Total	\$ 60.6	\$ 28.2	\$ 26.0

NOTE 13. UNAUDITED SELECTED QUARTERLY FINANCIAL DATA

The following tables summarize the unaudited quarterly financial data for the last two fiscal years:

	Fiscal 2014 Quarter Ended			
(in thousands, except per share data)	March 31,	June 30,	September 30,	December 31,
Total revenue	\$ 11,642	\$ 11,425	\$ 20,623	\$ 16,904
Total gross profit	2,676	3,126	13,162 (1)	4,438
Total operating expenses	20,921	21,428	21,575	22,332
Loss from operations	(18,245)	(18,302)	(8,413) (1)	(17,894)
Net loss	(18,886)	(19,136)	(9,163)	(18,975)
Basic and diluted net loss per share	\$ (0.28)	\$ (0.27)	\$ (0.13)	\$ (0.26)

	Fiscal 2013 Quarter Ended			
	March 31,	June 30,	September 30,	December 31,
Total revenue	\$ 5,578	\$ 6,048	\$ 7,421	\$ 9,134
Total gross profit	930	1,059	1,241	3,189
Total operating expenses	21,537	21,056	21,176	20,193
Loss from operations	(20,607)	(19,997)	(19,935)	(17,004)
Net loss	(21,104)	(20,471)	(20,487)	(17,231)
Basic and diluted net loss per share	\$ (0.37)	\$ (0.33)	\$ (0.31)	\$ (0.26)

- (1) During the third quarter ended September 30, 2014, we achieved the first development milestone as provided in the Roche Agreement and we recorded the related \$10.0 million as contractual revenue. See “Note 3. Contractual Revenue” for additional information.

ITEM 9A.CONTROLS AND PROCEDURES.

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our chief executive officer, our chief financial officer and our principal accounting officer, evaluated the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) of the Exchange Act) as of the end of the period covered by this Annual Report on Form 10-K. Based on this evaluation, our chief executive officer, chief financial officer and our principal accounting officer concluded that our disclosure controls and procedures were effective as of the end of the period covered by this report.

Management's Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Exchange Act Rules 13a-15(f). Under the supervision and with the participation of our management, including our Chief Executive Officer, Chief Financial Officer and Principal Accounting Officer, we conducted an evaluation of the effectiveness of our internal control over financial reporting based on the framework in Internal Control — Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) (COSO). Based on our evaluation under this framework our management concluded that our internal control over financial reporting was effective as of December 31, 2014.

Changes in Internal Control Over Financial Reporting

There were no changes in our internal control over financial reporting identified in connection with the valuation required by paragraph (d) of Exchange Act Rules 13a-15 or 15d-15 that occurred during our fourth fiscal quarter that have materially affected or are reasonably likely to materially affect, our internal control over financial reporting.

The effectiveness of our internal control over financial reporting as of December 31, 2014, has been audited by Ernst & Young LLP, our independent registered public accounting firm, as stated in their report which is included as follows.

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

The Board of Directors and Stockholders of Pacific Biosciences of California, Inc.

We have audited Pacific Biosciences of California, Inc.'s internal control over financial reporting as of December 31, 2014, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) (the COSO criteria). Pacific Biosciences of California, Inc.'s management is responsible for maintaining effective internal control over financial reporting, and for its assessment of the effectiveness of internal control over financial reporting included in the accompanying Management's Report on Internal Control Over Financial Reporting. Our responsibility is to express an opinion on the company's internal control over financial reporting based on our audit.

We conducted our audit in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects. Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

In our opinion, Pacific Biosciences of California, Inc. maintained, in all material respects, effective internal control over financial reporting as of December 31, 2014, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the 2014 consolidated financial statements of Pacific Biosciences of California, Inc. and our report dated March 12, 2015 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

Redwood City, California

March 12, 2015

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ITEM 9B.OTHER INFORMATION

None.

PART III

ITEM 10.DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE.

Information responsive to this item is incorporated herein by reference to our definitive proxy statement with respect to our 2015 Annual Meeting of Stockholders to be filed with the SEC within 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K.

ITEM 11.EXECUTIVE COMPENSATION.

Information responsive to this item is incorporated herein by reference to our definitive proxy statement with respect to our 2015 Annual Meeting of Stockholder Shareholders to be filed with the SEC within 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K.

ITEM 12.SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS.

Information responsive to this item is incorporated herein by reference to our definitive proxy statement with respect to our 2015 Annual Meeting of Stockholders to be filed with the SEC within 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K.

ITEM 13.CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE.

Information responsive to this item is incorporated herein by reference to our definitive proxy statement with respect to our 2015 Annual Meeting of Stockholders to be filed with the SEC within 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K.

ITEM 14.PRINCIPAL ACCOUNTING FEES AND SERVICES.

Information responsive to this item is incorporated herein by reference to our definitive proxy statement with respect to our 2015 Annual Meeting of Stockholders to be filed with the SEC within 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K.

PART IV

ITEM 15.EXHIBITS, FINANCIAL STATEMENT SCHEDULES.

(a)The following documents are filed as part of, or incorporated by reference into, this Annual Report on Form 10-K:

1. Financial Statements: See Index to Consolidated Financial Statements under Item 8 of this Annual Report on Form 10-K.
2. Financial Statement Schedules: All schedules are omitted because they are not required, are not applicable or the information is included in the consolidated financial statements or notes thereto.

3. Exhibits: We have filed, or incorporated by reference into this Annual Report on Form 10-K, the exhibits listed on the accompanying Exhibit Index immediately following the signature page of this Annual Report on Form 10-K.

(b)Exhibits: See Item 15(a)(3), above.

(c)Financial Statement Schedules: See Item 15(a)(2), above.

Signatures

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this Annual Report on Form 10-K to be signed on its behalf by the undersigned, thereunto duly authorized.

PACIFIC BIOSCIENCES OF CALIFORNIA, INC

By: /S/ SUSAN K. BARNES

Susan K. Barnes

Executive Vice President and Chief Financial Officer

Date: March 12, 2015

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below hereby constitutes and appoints Michael Hunkapiller, Susan K. Barnes and Brian B. Dow, and each of them, his or her true and lawful attorney-in-fact and agent, with full power of substitution, each with power to act alone, to sign and execute on behalf of the undersigned any and all amendments to this Annual Report on Form 10-K, and to perform any acts necessary in order to file the same, with all exhibits thereto and other documents in connection therewith with the Securities and Exchange Commission, granting unto said attorney-in-fact and agent full power and authority to do and perform each and every act and thing requested 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 attorney-in-fact and agent, or their or his or her substitutes, shall do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed by the following persons on behalf of the Registrant in the capacities and on the dates indicated.

Signature	Title	Date
/s/ Michael Hunkapiller	Executive Chairman, Chief Executive Officer and President	March 12, 2015
Michael Hunkapiller		
/s/ Susan K. Barnes	Executive Vice President and Chief Financial Officer	March 12, 2015
Susan K. Barnes		
/s/ Brian B. Dow	Vice President and Principal Accounting Officer	March 12, 2015
Brian B. Dow		
/s/ David Botstein	Director	March 12, 2015

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David Botstein

/s/ Brook Byers Director March 12,
2015

Brook Byers

/s/ William W. Ericson Director March 12,
2015

William W. Ericson

/s/ Randall S. Livingston Director March 12,
2015

Randall S. Livingston

/s/ John F. Milligan Director March 12,
2015

John F. Milligan

/s/ Marshall L. Mohr Director March 12,
2015

Marshall L. Mohr

/s/ Kathy Ordoñez Director March 12,
2015

Kathy Ordoñez

/s/ Lucy Shapiro Director March 12,
2015

Lucy Shapiro

Exhibit Index

		Incorporated by reference herein		
Exhibit Number	Description	Form	Exhibit No.	Filing Date
3.1	Amended and Restated Certificate of Incorporation	10-K	3.1	March 23, 2011
3.2	Amended and Restated Bylaws	10-K	3.2	March 23, 2011
4.1	Specimen Common Stock Certificate	S-1/A	4.1	October 1, 2010
4.2	Fifth Amended and Restated Investor Rights Agreement, dated June 16, 2010	S-1	4.2	August 16, 2010
4.3	Form of Warrant to purchase shares of common stock of the Registrant	8-K	4.1	February 5, 2013
10.1+	Form of Director and Executive Officer Indemnification Agreement	S-1	10.1	August 16, 2010
10.2+	2004 Equity Incentive Plan and forms of agreement thereunder	S-1	10.2	August 16, 2010
10.3+	2005 Stock Plan and forms of option agreements thereunder	S-1	10.3	August 16, 2010
10.4+	2010 Equity Incentive Plan and forms of option agreements thereunder	S-1	10.4	August 16, 2010
10.5+	2010 Employee Stock Purchase Plan and forms of agreement thereunder	S-1	10.5	August 16, 2010
10.6+	2010 Outside Director Equity Incentive Plan and forms of agreement thereunder	S-1	10.6	August 16, 2010
10.7†	Exclusive License Agreement by and between the Registrant and Cornell Research Foundation, Inc., dated as of February 1, 2004	S-1/A	10.8	October 22, 2010
10.8†	License Agreement by and between the Registrant and GE Healthcare Bio-Sciences Corp., dated as of September 11, 2006	S-1/A	10.9	October 22, 2010
10.9†	Exclusive License Agreement by and between the Registrant and Indiana University Research and Technology Corporation, dated May 15, 2005	S-1/A	10.10	October 19, 2010

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10.10	Amended and Restated Lease Agreement by and between the Registrant and Menlo Business Park, LLC, dated as of December 17, 2007	S-1	10.11	August 16, 2010
10.11	Lease Agreement by and between the Registrant and Menlo Business Park LLC, dated August 14, 2009	S-1	10.12	August 16, 2010
10.12	Industrial Lease Agreement by and between the Registrant and AMB Property, L.P., dated December 10, 2009	S-1	10.13	August 16, 2010
10.13	Third Amendment to the December 10, 2009 Industrial Lease by and between the Registrant and AMB Property, L.P. dated December 29, 2010	10-K	10.14	March 23, 2011
10.14	Industrial Lease Agreement by and between the Registrant and AMB Property, L.P., dated September 24, 2009	S-1	10.14	August 16, 2010
10.15	Third Amendment to the September 24, 2009 Industrial Lease by and between the Registrant and AMB Property, L.P. dated December 29, 2010	10-K	10.16	March 23, 2011
10.16	First Amendment to the September 24, 2009 Industrial Lease Agreement by and between the Registrant and AMB Property, L.P., dated as of May 19, 2010	S-1	10.15	August 16, 2010
10.17	Industrial Lease Agreement by and between the Registrant and AMB Property, L.P., dated February 8, 2010	S-1	10.16	August 16, 2010
10.18	First Amendment to the February 8, 2010 Industrial Lease by and between the Registrant and AMB Property, L.P. dated December 29, 2010	10-K	10.19	March 23, 2011
10.19	Lease by and between the Registrant and Willow Park Holding Company I, L.P. dated December 17, 2010	10-K	10.20	March 23, 2011
10.20	Lease by and between the Registrant and AMB Property, L.P. dated December 17, 2010	10-K	10.21	March 23, 2011

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10.21	Lease by and between the Registrant and Willow Park Holding Company II, L.P. dated December 17, 2010	10-K	10.21	March 23, 2011
10.22+	Letter Relating to Employment Terms by and between the registrant and Susan K. Barnes effective September 15, 2010	S-1/A	10.19	September 20, 2010
10.23+	Change in Control Severance Agreement by and between the registrant and Susan K. Barnes effective September 9, 2010	S-1/A	10.20	September 20, 2010
10.24+	Letter Relating to Employment Terms by and between the registrant and James Michael Phillips effective September 15, 2010	S-1/A	10.23	September 20, 2010
10.25+	Change in Control Severance Agreement by and between the registrant and James Michael Phillips effective September 9, 2010	S-1/A	10.24	September 20, 2010
10.26+	Employment Agreement by and between the registrant and Michael Hunkapiller dated January 5, 2012	10-K	10.32	March 1, 2012
10.27+	Change in Control Severance Agreement by and between the registrant and Michael Hunkapiller dated January 5, 2012	10-K	10.33	March 1, 2012
10.28	Controlled Equity Offering Sales Agreement, dated October 5, 2012, by and between the registrant and Cantor Fitzgerald & Co.	8-K	10.1	October 5, 2012
10.29	Amendment No. 1 to Controlled Equity Offering Sales Agreement, dated November 8, 2013, by and between the registrant and Cantor Fitzgerald & Co.	8-K	10.1	November 12, 2013
10.30	Amendment No. 2 to Controlled Equity Offering Sales Agreement, dated February 3, 2015, by and between the registrant and Cantor Fitzgerald & Co.	8-K	10.1	February 3, 2015
10.31+	Letter Agreement between the registrant and Michael Hunkapiller, dated December 14, 2012	8-K	10.1	December 14, 2012
10.32+	Letter Agreement between the registrant and Susan K. Barnes, dated December 14, 2012	8-K	10.2	December 14, 2012
10.33	Facility Agreement, dated February 5, 2013 by and among the Registrant and the entities listed on the signature pages thereof.	8-K	10.1	February 5, 2013
10.34	Security Agreement, dated February 5, 2013 by and among Pacific Biosciences of California, Inc. and the entities listed on the signature pages thereof.	8-K	10.3	February 5, 2013
10.35†	Development, Commercialization and License Agreement by and between the Registrant and F. Hoffman-La Roche Ltd. Dated September 24, 2013.	10-Q	10.1	November 12, 2013

- 12.1 Computation of Ratio of Earnings to Fixed Charges

- 23.1 Consent of Independent Registered Public Accounting Firm

- 31.1 Certification of Chief Executive Officer pursuant to Exchange Act Rules 13a-14(a) and 15d-14(a), as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002

- 31.2 Certification of Chief Financial Officer pursuant to Exchange Act Rules 13a-14(a) and 15d-14(a), as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002

- 32.1* Certification of Chief Executive Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002

- 32.2* Certification of Chief Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002

- 101.INS XBRL Instance Document

101.SCH XBRL Taxonomy Extension Schema Document

101.CAL XBRL Taxonomy Extension Calculation Linkbase Document

101.DEF XBRL Taxonomy Extension Definition Linkbase Document

101.LAB XBRL Taxonomy Extension Labels Linkbase Document

101.PRE XBRL Taxonomy Extension Presentation Linkbase Document

+Indicates management contract or compensatory plan

†Confidential treatment has been requested for portions of this exhibit. These portions have been omitted from this Registration Statement and have been filed separately with the Securities and Exchange Commission.

*The certifications attached as Exhibit 32.1 and 32.2 that accompany this Annual Report on Form 10-K are deemed furnished and not filed with the Securities and Exchange Commission and are not to be incorporated by reference into any filing of Pacific Biosciences of California, Inc. under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, whether made before or after the date of this Annual Report on Form 10-K, irrespective of any general incorporation language contained in such filing

