

PACIFIC BIOSCIENCES OF CALIFORNIA, INC.
Form 10-K
March 11, 2016

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

Form 10-K

(Mark One)

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

For the fiscal year ended December 31, 2015

Or

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

For the transition period from _____ to _____

Commission File Number 001-34899

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, 2015, based upon the closing price of Common Stock on such date as reported by NASDAQ Global Select Market, was approximately \$354,484,000. 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 7, 2016: 85,730,997

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 17, 2016 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 attributes and sequencing advantages of SMRT® technology and the Sequel™ System, market opportunities, strategic plans, including strategy for our business and related financing, expectations regarding the conversion of backlog to revenue and the pricing and gross margin for products, expectations regarding our collaboration agreements including the expected benefits of the Company’s agreement with Roche and the anticipated timing for Roche to release products, manufacturing plans including scaling of manufacturing of Sequel™ Systems and delivery of products, research and development plans, product development including, among other things, statements relating to future uses, quality or performance of, or benefits of using, products or technologies, updates or improvements of the company’s products, competition, expectations regarding unrecognized income tax benefits, expectations regarding the impact of an increase in market rates on the value of our investment portfolio, the sufficiency of cash, cash equivalents and investments to fund projected operating requirements, and the effects of recent accounting pronouncements on our financial statements and other future events. Such statements may be signified by terms such as “anticipates,” “believes,” “could,” “estimates,” “expects,” “intends,” “may,” “plans,” “potential,” “predicts,” “projects,” “seeks,” “should,” “target,” “will,” “would” or similar expressions and the like, and 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. Except as required by law, 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 sequencing systems to help scientists resolve genetically complex problems. Based on our novel Single Molecule, Real-Time (SMRT®) Sequencing 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 numerous peer-reviewed articles in journals including Nature, Science, Cell, PNAS and The New England Journal of Medicine highlighting the power and applications of SMRT sequencing 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 developing new products and further improving our existing products, including continuing chemistry and sample preparation improvements to increase throughput and expand our supported applications. By providing access to genetic information that was previously inaccessible, we enable 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 respectively. 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 organisms, the cytosine bases can be chemically modified through the addition of a methyl group in a process called methylation, resulting in modified bases such as 5-methylcytosine (5-mC) and N4-methylcytosine (4-mC). 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, 8-oxoguanine and many others, play important physiological roles. For example, in bacteria, N6-methyladenine (6-mA) 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 System and the Sequel™ System 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, scientists 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.

Sanger Sequencing

The first automated sequencing methodology, often referred to as “Sanger sequencing,” was 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 next-generation sequencing methods. However, Sanger sequencing is limited by the small amounts of data that can be processed per unit of time, referred to as throughput.

Short-read Sequencing

Several commercial DNA sequencing tools emerged in 2005 in response to the low throughput of Sanger sequencing. Now commonly referred to as “short-read sequencing”, these methods achieve much higher throughput by sequencing a large number of DNA molecules in parallel, but with the tradeoff of shorter read lengths.

In most short-read sequencing methodologies, 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 short-read sequencing methods can be longer, sometimes taking days. This repetitive process also limits the average read length produced by most of these systems under standard sequencing conditions to approximately 35 to 400 bases.

The short-read sequencing technologies require a large number of DNA molecules during the sequencing process. To generate enough DNA molecules, a copying method called PCR amplification is required during sample preparation. This amplification process can introduce errors known as amplification bias. The effect of this bias is that 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 summary, while short-read sequencing methods can offer very high throughput and low cost per identified base, their disadvantages can include limited read length, variation in sequence coverage with regard to representation bias and accuracy, dependence on amplification, long time to result, and/or a need for many samples to justify machine operation.

The PacBio Solution — Single Molecule, Real-Time Technology

We have developed our SMRT technology, which enables single molecule, real-time detection of biological processes, to address many of the limitations of previous sequencing technologies. By providing long read lengths, elimination of the dependence on amplification during sample preparation (which can result in amplification bias), very high consensus accuracy, and the ability to detect DNA base modifications, the PacBio RS II System and the Sequel System provide more comprehensive and higher quality information of DNA and RNA sequence as well as epigenetic regulation and DNA damage.

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 measuring approximately 15 nanometers (nm) in diameter, we offer three key innovations:

- The SMRT Cell
- Phospholinked nucleotides
- The PacBio RS II and Sequel instruments

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.

The ZMWs in our SMRT Cells consist of holes in an opaque layer, measuring only tens of nanometers in diameter forming nanoscale wells. 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, laser light shined into the ZMW from below is blocked from reaching the sequencing solution above the ZMW, providing selective illumination of only the bottom portion of the nanoscale well. DNA polymerases are anchored to the bottom of the glass surface of the nanoscale wells using proprietary techniques. 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 nanoscale wells, 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 provides 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 ZMWs. The SMRT Cells for the PacBio RS II System each contain approximately 150,000 ZMWs, whereas the SMRT Cells for the Sequel System each contain approximately one million 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 and Sequel Instruments

The PacBio RS II and Sequel instruments conduct, monitor, and analyze single molecule biochemical reactions in real time. The instruments use extremely sensitive imaging systems to collect the light pulses emitted by fluorescent reagents allowing the observation of biological processes. Computer algorithms are 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 previous 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

Users of SMRT technology can achieve very high consensus accuracy due to the attributes of SMRT sequencing, including long read lengths, lack of reliance on amplification during sample preparation (which can result in amplification bias), and lower systematic bias. Users of short-read 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 is compatible with but 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 sequence coverage. As a result, SMRT sequencing can detect and identify regions and entire genes that may be missed by short-read 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 and Sequel Systems 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 and Sequel Systems detect changes in kinetics automatically by capturing and recording changes in the duration of, and time period 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 6-mA, 4-mC and 5-mC. Other sequencing systems, which rely on a sample preparation amplification step or are limited by signal resolution, are unable to directly measure this type of kinetic data.

- Flexibility

Our sequencing systems have the ability to scale the throughput and cost of sequencing across a range of small to large projects. They 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 System, during the second quarter of 2011 and launched the higher performance PacBio RS II System during the second quarter of 2013. In September of 2015, we announced the Sequel System, which is based on the same underlying SMRT technology as the PacBio RS II System, but can achieve up to approximately seven times the throughput with newly-designed SMRT Cells. Our sequencing systems provide access to a wide range of applications and are designed for expandable improvements to performance capability and new application capabilities through chemistry and software enhancements without necessitating changes to instrument hardware.

PacBio Systems

The PacBio RS II and Sequel Systems conduct, monitor, and analyze biochemical sequencing reactions. The PacBio RS II and Sequel instruments are integrated units that include high performance optics, automated liquid handling, a touchscreen control interface and computational hardware and software. Each instrument's high performance optics monitor the ZMWs in a SMRT Cell in real time. The automated liquid handling system performs reagent mixing and

prepares SMRT Cells. Each instrument's touchscreen control interface is the user's primary control center to design and monitor experiments. The computational hardware and software in each instrument is responsible for processing the sequencing data produced by the SMRT Cells. Both the PacBio RS II System and the Sequel System have been designed to allow for performance improvements to be easily integrated into the systems.

Consumables

Customers must purchase proprietary consumable products to run either the PacBio RS II System or Sequel System. Our consumable products include our proprietary SMRT Cells and reagent kits. One SMRT Cell is consumed per sequencing reaction, and scientists can choose the number of SMRT Cells they use per experiment. For the PacBio RS II instrument, eight SMRT Cells containing approximately 150,000 ZMWs each are individually and hermetically sealed then packaged together into a streamlined 8Pac format. Sequel System customers purchase a similarly packaged, four SMRT Cell format with approximately one million ZMWs each.

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 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 contain reagents required for on-instrument, real-time sequencing, including the phospholinked nucleotides.

Product Enhancements

Since the introduction of our products in 2011, we have continued to significantly enhance the performance of PacBio sequencing systems through a combination of sample preparation protocol enhancements, software releases, and new sequencing reagent chemistries. By providing an increasing number of longer reads per instrument run, the new chemistries have enabled 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 2016, we plan to further improve our existing products, including chemistry and sample preparation improvements to increase throughput and expand our supported applications, and to continue 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 and RS II Systems 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 have 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 human leukocyte antigen, or HLA, genes. With the introduction of the Sequel System, our new higher throughput and lower cost platform for SMRT sequencing, we anticipate increasing both mindshare and market share within research and commercial markets such as human biomedical research, plant and animal sciences, 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

Key elements of our strategy include:

- 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 affords the scientific community a new tool to conduct research not possible with other sequencing technologies.

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

The design of our sequencing systems allows for significant performance improvements. Our flexible platforms are designed to generate a recurring revenue stream through the sale of proprietary SMRT Cells and reagent kits. We plan to introduce additional product enhancements over time to further reduce DNA sequencing project costs and time to result while expanding application solutions. During 2015, we introduced a new sequencing system called the Sequel

System as well as a variety of sample preparation improvements, and made significant enhancements to our software analysis toolkit. In addition, 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. With the introduction of the Sequel System, our new higher throughput and lower cost platform for SMRT sequencing, we anticipate increasing both market recognition and market share within the markets for our products. We plan to continue introducing enhancements to our products over time and to develop new products.

- 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, 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 help maximize the flexibility and functionality for users, our secondary analysis algorithms are made available under open source licenses. We also make available on our main corporate website various methods developed internally and externally for simplifying and enhancing sample preparation protocols.

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

We plan to leverage our customers' successes with SMRT sequencing to expand the capabilities of our products for applications our customers have identified as high-value based on the differentiating attributes of our technology. Early applications identified by our customers include: whole genome sequencing, targeted sequencing of complex regions, isoform discovery and characterization, resolution of complex populations, 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 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.

- Partner with Roche to sell to the in vitro diagnostics market.

In 2013, we entered into a collaboration agreement with F. Hoffman-La Roche Ltd ("Roche"), to jointly develop products based on our SMRT technology for the human in vitro diagnostics market. As a world leader in in vitro diagnostics, Roche brings valuable expertise in designing products for clinical use and obtaining regulatory approvals to sell clinical products in the U.S. and around the world. We believe the combination of our SMRT sequencing technology with Roche's market position and expertise in in vitro diagnostics will allow accelerated commercial success for both companies.

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 PacBio sequencing systems 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 the year ended December 31, 2015, 2014 and 2013, excluding contractual revenue, no single end customer accounted for more than 10% of our total revenue, respectively.

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. Roche related contractual revenue is classified as revenue from the United States. Revenue from customers outside the United States totaled \$24.9 million, or 27% of our total revenue during fiscal 2015, compared to \$26.2 million, or 43% of our total revenue, during fiscal 2014, and compared to \$14.6 million, or 52% of our total revenue, during fiscal 2013.

Backlog

As of December 31, 2015, our instrument backlog was approximately \$16.7 million, compared to \$8.4 million as of December 31, 2014. 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 2016; however, our ability to do so is subject to customers who may 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 /operating 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 expenses incurred were \$60.4 million, \$48.2 million and \$45.2 million during 2015, 2014 and 2013, respectively. We plan to continue our 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, 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, and will continue to seek, patent protection for our SMRT technology, for improvements to our SMRT technology, as well as for any of our other technologies where 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, 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, 2015, we own or hold exclusive licenses to 203 issued U.S. patents, 113 pending U.S. patent applications, 91 granted foreign patents and 85 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 our exclusively licensed 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. 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 milestone payments totaling \$40.0 million in 2014 and 2015 pursuant to the Roche Agreement. No further milestone payments are expected under the Roche Agreement. 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 trade secrets.

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, potentially competing technologies, products and/or services, including Oxford Nanopore Technologies Ltd. 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, the combination of very high consensus accuracy and long read lengths with the ability to detect real-time kinetic information, 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, 2015, we had 394 full-time employees. Of these employees, 146 were in research and development, 81 were in operations, 113 were in marketing, sales, service and support, and 54 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. As such, we have limited historical financial data upon which to base our projected revenue, planned operating expenses or upon which to evaluate our company and our commercial prospects. Furthermore, we recently launched a new nucleic acid sequencing platform, the Sequel™ System but have made only limited deliveries of the Sequel System to-date. 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, including the Sequel System;
 - 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, manufacture 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 any necessary 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. While we achieved profitability for the fiscal quarter ended September 30, 2015, this result was largely due to a one-time gain on lease amendments, we incurred a net loss for fiscal 2015, and,

even if profitability is achieved in the future, we may not be able to sustain profitability on a consistent basis. 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, including uses by academic, government and clinical laboratories, as well as pharmaceutical, diagnostic, biotechnology and agriculture companies, among others. 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 new and dynamic, and there can be no assurance that they will develop as quickly as we anticipate, that they will reach their full potential or that

they will be receptive to our recently-launched Sequel System. 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 across the full range of our intended life science and other applications. If the market for our products grows more slowly than anticipated, if we are unable to successfully scale the manufacturing of new products to meet demand, if competitors develop better or more cost-effective products or if we are unable to further grow our customer base, our current and future sales and revenue would be materially harmed and our business may not succeed.

If we are unable to successfully develop and timely manufacture our products, including Sequel Systems and related consumables, our business may be adversely affected.

In light of the highly complex technologies involved in our products, there can be no assurance that we will be able to manufacture and commercialize our new products on a timely basis or continue providing adequate support for our existing products. The commercial success of the Sequel System depends on a number of factors, including performance and reliability of the system, our anticipating and effectively addressing customer preferences and demands, the success of our sales and marketing efforts, effective forecasting and management of product demand, purchase commitments and inventory levels, effective management of manufacturing and supply costs, and the quality of the Sequel System, including related consumables such as SMRT Cells and reagents. Should we face delays in or discover unexpected defects during the further development or manufacturing process of Sequel instruments or consumables, including any delays or defects in software development or product functionality, the timing and success of the rollout of the Sequel System may be significantly impacted, which may materially and negatively impact our revenue and gross margin. The ability of our customers to successfully utilize the Sequel System will also depend on our ability to deliver high quality SMRT Cells and reagents. We have designed new SMRT Cells and other consumables for the Sequel System, which are being sourced from a prototype chip vendor, and we are in the process of transferring production to a high-volume manufacturer and may experience unanticipated delays or other issues. We anticipate that our yields on the manufacturing of the new SMRT Cells may initially be below desired levels and we may also experience manufacturing delays, product defects, or SMRT Cell variability, any of which could negatively impact our ability to sell Sequel Systems or result in other material adverse effects on our business, financial condition and results of operations.

The development of our products is complex and costly. Problems in the design or quality of our products may have a material and adverse effect on our brand, business, financial condition, and operating results, and could result in us losing our recently received certifications from the International Organization for Standardization (ISO). If we were to lose ISO certification, then our customers, including Roche, might choose not to purchase products from us. Unanticipated problems with our products could divert substantial resources, which may impair our ability to support our new and existing products, and could substantially increase our costs. If we encounter development challenges or discover errors in our products late in our development cycle, we may be forced to delay product shipments or the scaling of manufacturing or supply. In particular, if the rollout of the Sequel System is delayed or is not successful, we may not be able to achieve an acceptable return, if any, on our substantial research and development efforts, and our business may be materially and adversely affected. The expenses or losses associated with delayed or unsuccessful product development or lack of market acceptance of our new products could materially and adversely affect our business, financial condition and results of operations.

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

We entered into the Roche Agreement with Roche in September 2013, pursuant to which we are developing and expect to manufacture products for certain clinical research uses and, ultimately, for use in human in vitro diagnostics, including sequencing systems and consumables based on our proprietary SMRT technology and our Sequel System. We are engaged in substantial and complex 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 products we develop or supply under the Roche agreement. We could also be involved in disputes with Roche, which could lead to delays in or termination of our development and manufacture of products under the Roche Agreement 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 products developed or supplied under the Roche Agreement. If Roche terminates or breaches the Roche Agreement, or otherwise acquires, develops and/or commercializes alternative or competing products or services, the successful commercialization of our products for clinical uses would be materially and adversely affected.

Furthermore, we anticipate that Roche may account for a significant percentage of our total revenue in the future if they commercialize products developed or supplied under the Roche Agreement. As a consequence, we would see a concentration of our customer base, and Roche's purchasing behavior could cause our quarterly revenue and results of operations to fluctuate from quarter to quarter. For example, any cancellation of orders or any acceleration or delay in anticipated product purchases or the acceptance of

shipped products by Roche could materially affect our revenue and results of operations in any quarterly period. In such circumstances, the loss of Roche as customer, or a significant delay or reduction in their purchases, could materially harm our business, financial condition, results of operations and prospects.

We must successfully manage new product introductions and transitions, we may incur significant costs during these transitions, and they may not result in the benefits we anticipate.

If our products and services are not able to deliver the performance or results expected by our customers or potential customers, or are not delivered on a timely basis, our reputation and credibility may suffer, our current and future sales and revenue may be materially harmed and our business may not succeed. For instance, if we are not able to realize the benefits we anticipate from the development and commercialization of the Sequel System or our 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 the Sequel System and other 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. The introduction of new products, such as the Sequel System, may also have a negative impact on our revenue in the near-term as customers or potential customers may delay or cancel orders of existing products in anticipation of new products and we may also be required to decrease prices for our existing products. We may also experience difficulty in managing or forecasting customer reactions, purchasing decisions or transition requirements with respect to newly-launched products, such as the Sequel System. We could incur significant costs in completing the transition, including costs of inventory write-downs of RS II products, as customers or potential customers transition to the new Sequel System. If we do not successfully manage this product transition, our business, reputation and financial condition may be materially adversely harmed.

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. Furthermore, we are in the process of transferring production of the SMRT Cells for our Sequel System to a high-volume manufacturer and may experience unanticipated delays or other issues in connection with such transition. If we are required to purchase these components from alternative sources, 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, or if these components do not meet our expectations or specifications for quality and functionality, 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, including the Roche Agreement, 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 necessary specifications 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 expectations for quality and functionality in accordance with established specifications. Our customers have previously experienced variability in the performance of our instruments and SMRT Cells and we will be manufacturing a new version of our SMRT Cells for the Sequel System. We anticipate that our yields on the manufacturing of the new SMRT Cells may initially be below desired levels and we may also experience manufacturing delays, product defects, or SMRT Cell variability, especially as we transfer production of our SMRT Cells to a high-volume manufacturer. 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. Problems in the design or quality of our products may have a material adverse effect on our brand, business, financial condition, and operating results, and could result in us losing our recently received ISO certifications. If we were to lose ISO certification, then our customers, including Roche, might choose not to purchase products from us. 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 and components that consistently meet specifications, in necessary quantities and at commercially acceptable costs, will have a negative material impact on our business, financial condition and results of operations.

Rapidly changing technology in life sciences and diagnostics could make our products 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 the Sequel System and other new products could harm our future operating results. Unanticipated difficulties or delays in replacing existing products with new products or in commercializing the Sequel System or other new or improved 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 materially and 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. There are also several companies in the process of developing new, potentially competing technologies, products and/or services, including Oxford Nanopore Technologies Ltd. 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 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 our existing 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 partial payment of the notes. This right is subject to certain exceptions set forth in 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 partial payment of the notes.

Our products are highly complex, have recurring support requirements and 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 highly complex and may develop or contain undetected defects or errors. Our customers have in the past experienced reliability issues with our existing products, and we have only recently launched the Sequel System, so support costs are difficult to predict. Despite testing, defects or errors may arise in our products, which could result in a failure to maintain or increase market acceptance of our products, diversion of development resources, injury to our reputation and increased warranty, service and maintenance costs. New products or enhancements to our existing products in particular may contain undetected errors or performance problems that are discovered only after delivery to customers. 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 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 materially and adversely affect our operating margins. If our service and support costs increase, our business and operations may be materially and adversely affected.

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 materially 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 instruments represent significant capital expenditures 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 or if customers reconsider their orders, those customers may seek to cancel or modify their orders with us. 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 materially and 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, or those developed or supplied pursuant to our agreement with Roche, 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.

We currently conduct operations in various countries and jurisdictions. 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 materially and 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, such as the Foreign Corrupt Practices Act of 1977, as well as foreign laws relating to our activities in other countries, such as the United Kingdom Bribery Act of 2010. Failure to comply with these laws may subject us to financial and/or other penalties in the U.S. and/or foreign countries that could materially and adversely 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 or as a result of financial or other instability in such locations which could result in decreased sales of our products. 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 materially and adversely impact our financial condition and results of operations.

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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 represent a major capital expenditure 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. Sales to existing customers and the establishment of a business relationship with other potential customers is a lengthy process, generally taking several months and sometimes longer. Following the establishment of the relationship, the negotiation of purchase terms can be time-consuming, and a potential customer may require an extended evaluation and testing period. We cannot be sure what the sales cycle will be for the Sequel System. In

anticipation of product orders, we may incur substantial costs before the sales cycle is complete and before we receive any customer payments. As a result, in the event that a sale is not completed or is canceled or delayed, we may have incurred substantial expenses, making it more difficult for us to become profitable or otherwise negatively impacting our financial results. Furthermore, because of our lengthy sales cycle, the realization of revenue from our selling efforts may be substantially delayed, our ability to forecast our future revenue may be more limited and our revenue may fluctuate significantly from quarter to quarter.

Moreover, in previous quarters, we recognized substantial revenue derived from milestone payments under the Roche Agreement. All of the milestones under the Roche Agreement have now been achieved, however, which may significantly affect our quarterly operating results in fiscal 2016, particularly during the periods in which our sales volume is low. Because of this, it is possible that in some future quarters our operating results will fall below the expectations of securities analysts or investors, which may negatively impact the market price of our common stock.

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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.

Our ability to successfully manage our transition to our new headquarters could result in a material adverse effect on our business or operations if we underestimate the costs of the transition, experience delays or quality issues with our manufacturing, or if internal measures to mitigate these risks are not effective.

We are in the process of transitioning to our new headquarters in Menlo Park, California. The successful transition of our headquarters, including the transition of our manufacturing facilities, is largely dependent upon the cooperation and continued performance of both our current and future landlords, as well as third-party contractors who are preparing certain shell improvements and tenant improvements. During the transition period, we must establish procedures to ensure that our current and future manufacturing facilities meet our quality standards while maintaining a reasonable cost structure. In addition, after our new manufacturing facilities have been qualified, it may take a considerable period of time to commence volume production. We have already devoted significant expenses and resources in connection with the transition, and there is no assurance that we can manage the transition successfully. If the transition does not go as expected, in addition to other issues noted above, we could experience delayed shipments

of products, unexpected cost overruns or quality issues, or loss of our ISO certifications, each of which could have a material adverse effect on our business, operating results and business reputation. In addition, in the event that we breach any of our current Menlo Park facility real property leases and fail to cure such breach within the time permitted, the landlord would have no obligation to make the final \$5.0 million payment due to us under the leases, as amended, as consideration for our agreement to amend the leases.

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 materially and 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 products 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 materially and 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 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.

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 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 in these proceedings may negatively impact the scope of our intellectual property protection for our products and technology and may materially and 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. Furthermore, 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. Furthermore, parties making claims against us may be able to obtain injunctive or other relief, which effectively could block our ability to develop further, commercialize, or sell products or services, and could result in the award of substantial damages against us. 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 that we 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 being prevented from selling some or all of our products, which could materially and 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 or otherwise materially and 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 or 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 foregoing 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 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 have resulted and will continue to result in dilution of our existing stockholders, and such sales could cause our stock price to fall.

In addition, if our existing stockholders sell, or indicate an intent to sell, a large number of shares of our common stock in the public market, it could cause our stock price to fall. We may also issue shares of common stock or securities convertible into our common stock from time to time in connection with financings, acquisitions, investments or otherwise. Any such issuance would result in dilution to our existing stockholders and could cause our stock price to fall.

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 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 dividends on our common stock and do not intend to pay any 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. In July 2015 we amended the terms and conditions of our existing Menlo Park facility real property leases to, among other things, extend the terms of certain of the leases, with one lease continuing to expire in December 2015, one lease now expiring in December 2016 and the remainder now expiring in September 2017. As of January 1, 2016 we lease approximately 172,000 square feet under the amended Menlo Park facility real property leases. We also lease a sales office facility in Singapore, and engineering support facilities in San Francisco, California.

In addition, in July 2015 we entered into a new lease agreement (the "O'Brien Lease") with respect to our proposed new premises at 1315 O'Brien Drive, Menlo Park, California (the "O'Brien Premises"). The term of the O'Brien Lease is one hundred thirty-two (132) months, commencing on the date that is the later of April 15, 2016 or the date on which the O'Brien Premises landlord has substantially completed certain shell improvements and tenant improvements. However, if any delay in the construction schedule is attributable to us under the lease, the lease will commence on the date substantial completion would have occurred but for the delay. Based on the currently agreed construction schedule, the O'Brien Lease will commence no earlier than June 1, 2016 and we believe that substantial completion will occur no earlier than August 1, 2016.

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.

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.

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 sales prices per share for our common stock for the indicated fiscal periods:

	2015		2014	
	High	Low	High	Low
4th Quarter	\$ 14.00	\$ 4.26	\$ 8.10	\$ 4.52
3rd Quarter	5.90	3.58	6.42	4.38
2nd Quarter	6.55	5.11	6.65	3.87
1st Quarter	8.78	5.38	8.20	4.73

Holders of Record

As of March 7, 2016, there were approximately 46 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, 2015 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
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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	19,467,724	\$ 5.69	5,503,848
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 December 2010 through December 31, 2015 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.

	12/2010	12/2011	12/2012	12/2013	12/2014	12/2015
Pacific Biosciences of California, Inc.	\$ 100.00	\$ 17.60	\$ 10.69	\$ 32.87	\$ 49.28	\$ 82.53
NASDAQ Composite Index	100.00	100.53	116.92	166.19	188.78	199.95
NASDAQ Biotechnology Index	100.00	113.92	153.97	263.29	348.49	369.06

Recent Sales of Unregistered Securities

None.

Use of Proceeds

On October 5, 2012, we entered into a sales agreement pursuant to which we sold shares of our common stock having an aggregate offering price of approximately \$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 available for sale pursuant to the sales agreement, and pursuant to such amendment, we sold an additional aggregate offering price of approximately \$30.0 million. On February 3, 2015, the sales agreement

was amended again in order to further increase the shares of our common stock available for sale pursuant to the sales agreement, and, pursuant to such amendment, we sold an additional aggregate offering price of approximately \$30.0 million. On February 3, 2016 we filed a prospectus supplement pursuant to which we may offer and sell, from time to time, additional shares of our common stock having an aggregate offering price of up to \$30.0 million under the sales agreement. Such aggregate offering price of shares of our common stock is in addition to the shares sold under the original sales agreement, dated October 5, 2012, the first amendment to such sales agreement, dated November 8, 2013, and amounts previously sold under the second amendment to such sales agreement, dated February 3, 2015. 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, 2015, we have sold a total of 18.1 million shares of our common stock at an average price of \$4.96 through our “at-the-market” offering, for total net proceeds of \$87.3 million.

From January 1, 2016 to March 7, 2016, we issued 2.7 million shares of our common stock at an average price of \$8.79 per share through our “at-the-market” offering, resulting in net proceeds of \$23.4 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,				
	2015	2014	2013	2012	2011
	(in thousands except per share amounts)				
Total revenue (1)(2)	\$ 92,782	\$ 60,594	\$ 28,181	\$ 25,983	\$ 33,863
Total cost of revenue (1)	39,332	37,192	21,762	25,043	20,829
Gross profit (1)	53,450	23,402	6,419	940	13,034
Gain on lease amendments (3)	(23,043)	—	—	—	—
Total operating expense	82,584	86,256	83,962	95,278	122,790
Operating loss	(29,134)	(62,854)	(77,543)	(94,338)	(109,756)
Net loss	\$ (31,696)	\$ (66,160)	\$ (79,293)	\$ (94,465)	\$ (109,388)
Net loss per share:					
Basic and diluted net loss per share	\$ (0.42)	\$ (0.94)	\$ (1.26)	\$ (1.69)	\$ (2.03)
Shares used in computing basic and diluted net loss per share (4)	75,614	70,475	62,784	55,733	53,874
	As of December 31,				
	2015	2014	2013	2012	2011
	(in thousands)				

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Cash, cash equivalents and investments	\$ 82,270	\$ 101,348	\$ 112,528	\$ 100,580	\$ 177,434
Working capital	72,363	86,271	103,904	100,257	180,225
Total assets	131,107	124,390	136,036	129,683	218,316
Total liabilities (5)	57,567	69,441	66,856	20,301	26,853
Total stockholders' equity (4)	\$ 73,540	\$ 54,949	\$ 69,180	\$ 109,382	\$ 191,463

- (1) We began recording product and service revenue and the related cost of revenue in 2011 from sales of our 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 the Roche Agreement and received a non-refundable up-front payment of \$35.0 million. Revenue for the year ended December 31, 2014 consists of four quarterly periods of amortization of \$1.7 million from the non-refundable up-front payment of \$35.0 million, while revenue for the year ended December 31, 2015 consists of four quarterly periods of amortization of \$3.6 million, reflecting the increased certainty of the development time period. In addition, we achieved the first development milestone under the Roche Agreement and recorded the related \$10.0 million as contractual revenue during the year ended December 31, 2014. We achieved the second and third (final) development milestones under the Roche Agreement and recognized the related \$10.0 million and \$20.0 million, respectively, as contractual revenue during the year ended December 31, 2015. Please see "Note 3. Contractual revenue" in Part II, Item 8 of this Form 10-K for additional information.

- (3) Comprised of one-time gain of \$23.0 million associated with the lease amendment agreements with our existing landlord, which amended the terms and conditions of certain of our existing Menlo Park facility real property leases. Please see “Note 7. Commitments and contingencies” in Part II, Item 8 of this Form 10-K for additional information.
- (4) From 2012 to 2016 we established various “at-the-market” offerings pursuant to which we could offer and sell shares of our common stock. Our first sales through our “at-the-market” offering occurred in 2013 and as of December 31, 2015, we have sold a total of 18.1 million shares of our common stock at an average price of \$4.96, for total net proceeds of \$87.3 million. Please see “Note 9. Stockholders’ equity” in Part II, Item 8 of this Form 10-K for additional information.
- (5) 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 sequencing systems to help scientists resolve genetically complex problems. Based on our novel Single Molecule, Real-Time (SMRT®) Sequencing 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.

In September 2015, we announced that we had launched a new nucleic acid sequencing platform, the Sequel System, which will provide higher throughput, more scalability, a reduced footprint and lower sequencing project costs compared to the PacBio® RS II System, while maintaining the existing benefits of our SMRT Technology.

2015 Business Events and Trends

Product Developments. During September 2015, we announced a new nucleic acid sequencing platform, the Sequel System, which will provide higher throughput, more scalability, a reduced footprint and lower sequencing project costs compared to the PacBio RS II System, while maintaining the existing benefits of our SMRT Technology. The core of the Sequel System is the capacity of its redesigned SMRT Cells, which contain approximately one million zero-mode waveguides (ZMWs) at launch, compared to approximately 150,000 ZMWs in the PacBio RS II System. The Sequel System has been developed as part of our collaboration with Roche to ultimately provide a nucleic acid sequencing system for use in human in vitro diagnostics. We began limited shipments of the Sequel System in the United States during the fourth quarter of 2015 and expect to begin scaling the manufacturing process for the Sequel Systems and the new SMRT Cells during early 2016.

Diagnostic Collaboration with Roche. During September 2013, we entered into the Roche Agreement with Roche, pursuant to which we account for, and recognize as revenue, a \$35.0 million up-front payment we received upon entering into the Roche Agreement using the proportional performance method over the periods in which the delivery of elements pursuant to the Roche 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 Roche Agreement. Effective January 1, 2015, we revised the amortization period based on increased certainty of the estimated development time period and recognized additional revenue of \$1.9 million per quarter and a total of an additional \$7.6 million of revenue for the year ended December 31, 2015. In addition to the above upfront payment, the Roche Agreement provides for additional payments totaling up to \$40.0 million upon the achievement of certain milestones. During August 2014, we achieved the first such development milestone and recorded the related \$10.0 million as contractual revenue for the quarter ended September 30, 2014. During April 2015, we achieved the second development milestone and recognized the related \$10.0 million as contractual revenue for the quarter ended June 30,

2015. During November 2015, we achieved the third (final) development milestone and recognized the related \$20.0 million as contractual revenue in the fourth quarter of 2015.

Cash Position. Cash, cash equivalents and investments, excluding restricted cash, at December 31, 2015 totaled \$82.3 million, compared to \$101.3 million at December 31, 2014. During 2015, we received \$29.1 million, net, 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 the receipt of cash related to contractual revenue as well as any additional funds raised. From January 1, 2016 to March 7, 2016, we issued 2.7 million shares of our common stock at an average price of \$8.79 per share through our “at-the-market” offering, resulting in net proceeds of \$23.4 million.

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 (“U.S. 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, instrument lease 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. For certain qualified distributors revenue is recognized based upon shipment terms. 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.

For instrument lease agreements we entered into with our customers so far, they are classified as operating-type leases and revenue from these leases is recognized on a straight-line basis over the respective lease term, once the lessee takes (or has the right to take) control/possession of the property under the lease. Effectively, this occurs once installation is complete and acceptance has been obtained.

We 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

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Inventory is valued at the lower of standard cost, which approximates actual cost, or market. Cost is determined using the first-in, first-out (“FIFO”) 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 U.S. 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, 2015, we maintained a full valuation allowance against all of our deferred tax assets which totaled \$285.6 million, including net operating loss carryforwards and research and development tax credits of \$235.7 million and \$28.3 million, respectively. Our deferred tax assets include federal and state net operating loss carryforwards of approximately \$612.9 million and \$523.4 million, respectively, and federal and state research and development credit carryforwards of approximately \$23.9 million and \$25.6 million, respectively. The federal net operating loss carryforward begins expiring in 2024, the state net operating loss carryforward have expirations in 2015 and beyond, the federal research and development credits begin expiring in 2024 and 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

Recently Adopted Accounting Standards

In November 2015, the FASB issued ASU 2015-17, Income Taxes: Balance Sheet Classification of Deferred Taxes, which requires that deferred tax assets and liabilities be classified as noncurrent on the consolidated balance sheet. ASU 2015-17 is effective for fiscal years, and interim periods within those years, beginning after December 15, 2016. Early adoption is permitted, and the standard may be applied either retrospectively or on a prospective basis to all deferred tax assets and liabilities, and we have elected to early adopt ASU 2015-17 prospectively, effective for the year ended December 31, 2015, as permitted by the standard. The early adoption of this update did not have a material impact on our consolidated financial statements.

In April 2015, the Financial Accounting Standards Board (“FASB”) issued Accounting Standards Update (“ASU”) 2015-03, Simplifying the Presentation of Debt Issuance Costs, which changes the presentation of debt issuance costs in financial statements. ASU 2015-03 requires an entity to present such costs in the consolidated balance sheet as a direct deduction from the related debt liability rather than as an asset. Amortization of the costs will continue to be reported as interest expense. ASU 2015-03 is effective for annual reporting periods beginning after December 15, 2015 and is effective for us in the first quarter of fiscal 2016. Early adoption is permitted, and we elected to apply the new guidance retrospectively to each prior period presented, as permitted by the standard. Early adoption is also permitted for financial statements that have not been previously issued, and we elected to early adopt the accounting standard for the year ended December 31, 2015, as permitted by the standard. The early adoption of ASU 2015-03 did not have a material impact on the consolidated statements of operations and comprehensive loss. The impact of early adoption on the consolidated balance sheets for the periods presented is noted in the table below (in thousands):

(in thousands)	December 31, 2015			December 31, 2014		
	Prior to Adoption of ASU 2015-03	ASU 2015-03 Adjustment	As adopted	Prior to Adoption of ASU 2015-03	ASU 2015-03 Adjustment	As adopted
Other long-term assets	\$ 7,631	\$ (113)	\$ 7,518	\$ 162	\$ (133)	\$ 29
Total assets	7,631	(113)	7,518	162	(133)	29
Notes payable	15,061	(113)	14,948	14,124	(133)	13,991
Total liabilities	\$ 15,061	\$ (113)	\$ 14,948	\$ 14,124	\$ (133)	\$ 13,991

Recently Issued Accounting Standards

In February 2016, the FASB issued ASU 2016-02, Leases. The guidance in ASU 2016-02 supersedes the lease recognition requirements in ASC Topic 840, Leases. ASU 2016-02 requires an entity to recognize assets and liabilities arising from a lease for both financing and operating leases, along with additional qualitative and quantitative

disclosures. ASU 2016-02 is effective for fiscal years beginning after December 15, 2018, with early adoption permitted. We are currently evaluating the new guidance to determine the impact it may have to our consolidated financial statements.

In July 2015, the FASB issued ASU 2015-11, Simplifying the Measurement of Inventory, which simplifies the subsequent measurement of inventory by replacing today's lower of cost or market test with a lower of cost and net realizable value test. The guidance applies only to inventories for which cost is determined by methods other than last-in first-out (LIFO) and the retail inventory method (RIM). Entities that use LIFO or RIM will continue to use existing impairment models (e.g., entities using LIFO would apply the lower of cost or market test). ASU 2015-11 is effective for annual report periods beginning after December 15, 2016 and is effective for us in the first quarter of 2017. Early adoption is permitted as of the beginning of an interim or annual reporting period. The new guidance must be applied prospectively after the date of adoption. The adoption of ASU 2015-11 is not expected to have a material impact on our consolidated financial statements.

In May 2014, the FASB issued ASU 2014-09, Revenue from Contracts with Customers, requiring an entity to recognize the amount of revenue to which it expects to be entitled 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 the retrospective or cumulative effect transition method. In August 2015, the FASB issued ASU 2015-14, Revenue from Contracts with Customers: Deferral of the Effective Date, which deferred the effective date of the new revenue standard for periods beginning after December 15, 2016 to December 15, 2017, with early adoption permitted but not earlier than the original effective date. Accordingly, the updated standard is effective for us in the first quarter of 2018. We are currently evaluating the new guidance to determine the impact it may have to our consolidated financial statements.

Results of Operations

Comparison of the Years Ended December 31, 2015 and 2014

	Year Ended December 31,			
	2015	2014	\$ Change	% Change
Revenue:	(in thousands, except percentages)			
Product revenue	\$ 37,502	\$ 35,299	\$ 2,203	6%
Service and other revenue	10,896	8,511	2,385	28%
Contractual revenue	44,384	16,784	27,600	164%
Total revenue	92,782	60,594	32,188	53%
Cost of Revenue:				
Cost of product revenue	30,704	29,626	1,078	4%
Cost of service and other revenue	8,628	7,566	1,062	14%
Total cost of revenue	39,332	37,192	2,140	6%
Gross profit	53,450	23,402	30,048	128%
Operating Expense:				
Research and development	60,440	48,230	12,210	25%
Sales, general and administrative	45,187	38,026	7,161	19%
Gain on Lease amendments	(23,043)	—	(23,043)	
Total operating expense	82,584	86,256	(3,672)	(4%)
Operating loss	(29,134)	(62,854)	33,720	54%
Interest expense	(2,926)	(2,828)	(98)	(3%)
Other income (expense), net	364	(478)	842	176%
Net loss	\$ (31,696)	\$ (66,160)	\$ 34,464	52%

Revenue

	Year Ended		\$ Change	% Change
	2015	2014		
Revenue:	(in thousands, except percentages)			
Instrument revenue	\$ 18,728	\$ 22,125	\$ (3,397)	(15%)
Consumable revenue	18,774	13,174	5,600	43%
Total product revenue	37,502	35,299	2,203	6%
Service and other revenue	10,896	8,511	2,385	28%
Contractual revenue	44,384	16,784	27,600	164%
Total revenue	\$ 92,782	\$ 60,594	32,188	53%

Total revenue for the year ended December 31, 2015 was \$92.8 million compared to \$60.6 million for 2014.

Product revenue for the year ended December 31, 2015 consisted of \$18.7 million from sales of instruments and \$18.8 million from sales of consumables, compared to \$22.1 million from sales of instruments and \$13.2 million from sales of consumables for the year ended December 31, 2014. The decrease in sales of instruments from 2014 to 2015 included the effects of the product transition from the PacBio RS II System to the Sequel System. The increase in consumable sales from 2014 to 2015 was primarily attributable to a

larger installed instrument base and higher utilization of installed instruments by our customers. We expect product revenue to be relatively flat in the early part of 2016, and to then increase significantly during the remainder of the year assuming we increase shipments of Sequel Systems.

Service and other revenue for the year ended December 31, 2015 primarily consisted of service revenue of \$10.9 million compared to service revenue of \$8.5 million for the year ended December 31, 2014. Service revenue was, and continues to be, derived from product maintenance agreements sold on our installed instruments. The increase in service revenue from 2014 to 2015 was primarily attributable to a larger installed instrument base in 2015.

Contractual revenue includes \$14.4 million and \$6.8 million for the years ended December 31, 2015 and 2014, respectively, from the amortization of the non-refundable up-front payment of \$35.0 million we received during September 2013 pursuant to the Roche Agreement. Contractual revenue for 2015 included an additional \$7.6 million, compared to the prior year, reflecting the increased certainty of the estimated development time period. We achieved the first development milestone under the Roche Agreement and recorded the related \$10.0 million as contractual revenue during the year ended December 31, 2014. We achieved the second and third (final) development milestones under the Roche Agreement and recognized the related \$10.0 million and \$20.0 million, respectively, as contractual revenue during the year ended December 31, 2015. We expect contractual revenue to decrease in 2016, as there are no remaining development milestones associated with the Roche Agreement to be recognized, and the remaining amortization of the up-front payment of \$35.0 million is scheduled to decrease significantly in the fourth quarter of 2016.

Gross Profit

Gross profit for the year ended December 31, 2015 totaled \$53.5 million, resulting in a gross margin of 57.6%, compared to a \$23.4 million gross profit for the year ended December 31, 2014 and a gross margin of 38.6%. Both gross profit and gross margin in 2015 have increased over 2014 as a result of the growth described above in consumable revenue, which has higher margins, and in contractual revenue, which has a gross margin of 100%.

Cost of product revenue increased to \$30.7 million for the year ended December 31, 2015, compared to cost of product revenue of \$29.6 million for 2014. The increase in cost of product revenue was primarily driven by the growth of consumable shipments.

Cost of service and other revenue for the year ended December 31, 2015 increased to \$8.6 million compared to \$7.6 million for the year ended December 31, 2014. The cost of service and other revenue increased in line with the growth in revenue but was partially offset by leveraging existing infrastructure.

Gross margin for 2016 is expected to be lower than 2015, as there are no remaining development milestones associated with the Roche Agreement to be recognized. Quarterly gross margin in 2016 is expected to be variable depending on the revenue mix, including the amount of contractual revenue recognized and the amount of product revenue associated with Roche, which is expected to have lower gross margin than product revenue associated with other customers, based on lower distributor prices to Roche.

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, 2015, research and development expenses increased \$12.2 million, or 25%, compared to the year ended December 31, 2014. The increase in research and development expenses was primarily attributed to an increase of \$6.7 million in product development costs related to the launch of the Sequel System and higher compensation related expenses resulting from increased headcount and higher stock-based compensation expenses. Research and development expenses included stock-based compensation expenses of \$5.2 million and \$3.8 million for the years ended December 31, 2015 and 2014, respectively. We expect our total research and development expenses for 2016 to be similar to 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.

For the year ended December 31, 2015, sales, general and administrative expenses increased \$7.2 million, or 19%, compared to the year ended December 31, 2014. The increase in sales, general and administrative expenses was primarily attributed to an increase of \$5.3 million in compensation related expenses resulting from increased headcount and higher stock-based compensation expenses and an increase of \$2.1 million in professional fees, of which \$1.2 million was primarily related to fees associated with the final Roche milestone payment of \$20.0 million recognized during the fourth quarter of 2015. Sales, general and administrative expenses included

stock-based compensation expenses of \$7.3 million and \$5.4 million for the years ended December 31, 2015 and 2014, respectively. We expect our sales, general and administrative expenses to increase in 2016.

Gain on Lease Amendments

On July 23, 2015, we entered into a Lease Amendment Agreement (the “Lease Amendment Agreement”) with Peninsula Innovation Partners, LLC (the “Existing Landlord”), which amends the terms and conditions of certain of our existing Menlo Park facility real property leases. The Lease Amendment Agreement provides for, among other things, amendments of the term for certain of the existing leases, the termination of all renewal, expansion and extension rights contained in any of the existing leases with the Existing Landlord (including our options to extend the terms for certain of the existing leases for two consecutive five-year periods), as well as rent abatement for a specified period of time. As consideration for our agreement to amend the existing leases pursuant to the Lease Amendment Agreement, and subject to the terms and conditions contained therein, we are eligible to receive up to four payments of \$5.0 million each from the Existing Landlord over time (the “Landlord Payments”), and rent abatement for the remainder of the lease. In the event that we breach any of the leases and fail to cure such breach within the time permitted, the Existing Landlord would have no obligation to make the final \$5.0 million payment. On September 1, 2015 the permitting process related to an architectural approval and a change of use permit with respect to the O’Brien Premises was completed and the related contingencies satisfied. As a result, we recorded \$23.0 million in “Gain on lease amendments” in the consolidated statements of operations and comprehensive loss for the year ended December 31, 2015, reflecting that our rent payments were reduced to zero for the remaining term of our existing Menlo Park facility real property leases, the aggregate of \$20.0 million in Landlord Payments became receivable and any associated financing obligation was revalued.

Interest Expense

Interest expense for the year ended December 31, 2015 remained flat compared to 2014. Interest expense related primarily to the debt facility entered into in February 2013.

Comparison of the Years Ended December 31, 2014 and 2013

	Year Ended December			
	2014	2013	\$ Change	% Change
	(in thousands, except percentages)			
Revenue:				
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			
	2014	2013	\$ Change	% Change
	(in thousands, except percentages)			
Revenue:				
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.

Research and Development Expense

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.

Sales, General and Administrative Expense

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.

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.

Liquidity and Capital Resources

Liquidity

Since our inception, we have financed our operations primarily through product sales, issuance of common stock and convertible preferred stock, in addition to our debt facility and payments from Roche pursuant to the terms of the Roche Agreement. Cash, cash equivalents and investments, excluding restricted cash, at December 31, 2015 totaled \$82.3 million, compared to \$101.3 million at December 31, 2014.

We believe that our 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, including our current “at-the-market” offering, 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 and our collaboration agreement with Roche; 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; the costs associated with the transition to our new facilities in Menlo Park, California; 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 flow activities for the periods indicated.

(in thousands)	Year Ended December 31,		
	2015	2014	2013
Net cash provided by (used in):			
Operating activities	\$ (47,889)	\$ (51,468)	\$ (29,833)
Investing activities	8,606	19,564	(33,117)
Financing activities	36,463	41,991	42,772

Operating Activities

Our primary uses of cash in operating activities are for the development of ongoing product enhancements and future products, manufacturing, and support functions related to our selling, general and administrative activities. The net cash used for the years ended December 31, 2015, 2014 and 2013 primarily reflected the net loss for those periods, partially offset by non-cash operating expenses including depreciation and stock-based compensation, and also reflected changes in working capital.

Cash used in operating activities of \$47.9 million in 2015 reflected a net loss of \$31.7 million, adjusted for non-cash items such as stock-based compensation of \$13.8 million, depreciation and amortization of \$3.7 million, the non-cash portion relating to the gain on lease amendments of \$3.0 million, and amortization of debt discount and financing costs of \$1.0 million. Additionally, the change in net operating assets and liabilities was attributed to an increase of prepaid expenses and other assets of \$17.9 million, of which a \$15.0 million increase related to the future Landlord Payments associated with the Lease Amendment Agreement, a reduction in deferred contractual revenue of \$14.4 million and a decrease in inventory of \$2.5 million, offset by an increase of \$5.0 million of accounts payable and accrued expenses due primarily to the timing of payments. The change in inventory also reflects a transfer of \$2.8 million from inventory to fixed assets relating to PacBio RS II instrument leasing arrangements.

Cash used in operating activities of \$51.5 million in 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 an increase of \$3.9 million in accounts payable and an increase of \$3.5 million in accrued expenses, partially offset by a decrease of \$6.8 million in deferred contractual revenue

during 2014.

Cash used in operating activities of \$29.8 million in 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 an increase of \$33.3 million of deferred development revenue associated with the Roche Agreement.

Investing Activities

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

In 2015, net cash provided by investing activities was \$8.6 million, comprised of \$16.1 million in net maturities and sales of investments, partially offset by \$3.0 million in net purchases of property and equipment, and \$4.5 million in long-term restricted cash related to a letter of credit established in October 2015 for O'Brien Lease Agreement.

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

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

Financing Activities

In 2015, cash provided by financing activities was \$36.5 million, comprised of net proceeds of \$29.1 million from our common stock "at-the-market" offering and \$7.4 million from the issuance of common stock through our equity compensation plans.

In 2014, cash provided by financing activities was \$42.0 million, comprised of net proceeds of \$38.0 million from our common stock “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 our equity compensation plans.

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. We have \$30 million of common stock available for future sales under our common stock “at-the-market” offering; however, we are not obligated to make any sales of shares of our common stock under this program.

Debt Facility 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, and the facility agreement has a maximum term of seven years. 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, the Facility Agreement requires us 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.

Subject to certain exceptions set forth in the Facility Agreement, holders representing a majority of the aggregate principal amount of the outstanding Notes issued pursuant to the Facility Agreement may elect to receive 25% of the net proceeds from any financing that includes an equity component, including without limitation, sales pursuant to our common stock “at-the-market” offering. To the extent we raise additional capital in the future through the sale of common stock under our current “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 partial payment of the Notes.

Common Stock “At-the-Market” Offering

On October 5, 2012, we entered into a sales agreement pursuant to which we sold shares of our common stock having an aggregate offering price of approximately \$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 available for sale pursuant to the sales agreement, and, pursuant to such amendment, we sold an additional aggregate offering price of approximately \$30.0 million. On February 3, 2015, the sales agreement was amended again in order to further increase the shares of our common stock available for sale pursuant to the sales agreement, and, pursuant to such amendment, we sold an additional aggregate offering price of approximately \$30.0 million. On February 3, 2016 we filed a prospectus supplement pursuant to which we may offer and sell, from time to time, additional shares of our common stock having an aggregate offering price of up to \$30.0 million under the sales agreement. Such aggregate offering price of shares of our common stock is in addition to the shares sold under the original sales agreement, dated October 5, 2012, the first amendment to such sales agreement, dated November 8, 2013, and amounts previously sold under the second amendment to such sales agreement, dated February 3, 2015. 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, 2015, we have sold a total of 18.1 million shares of our common stock at an average price of \$4.96 through our “at-the-market” offering, for total net proceeds of \$87.3 million.

From January 1, 2016 to March 7, 2016, we issued 2.7 million shares of our common stock at an average price of \$8.79 per share through our “at-the-market” offering, resulting in net proceeds of \$23.4 million.

Contractual Obligations, Commitments and Contingencies

Lease Amendment Agreement

On July 23, 2015, we entered into the Lease Amendment Agreement with the Existing Landlord, which amends the terms and conditions of certain of our existing Menlo Park facility real property leases. The Lease Amendment Agreement provides for, among other things, amendments of the term for certain of the existing leases, the termination of all renewal, expansion and extension rights contained in any of the existing leases with the Existing Landlord (including our options to extend the terms for certain of the existing leases for two consecutive five-year periods), as well as rent abatement for a specified period of time. As consideration for our agreement to amend the existing leases pursuant to the Lease Amendment Agreement, and subject to the terms and conditions contained therein, we are eligible to receive the Landlord Payments, and rent abatement for the remainder of the lease. In the event that we breach any of the leases and fail to cure such breach within the time permitted, the Existing Landlord would have no obligation to make the final \$5.0 million payment. On September 1, 2015 the permitting process related to an architectural approval and a change of use permit with respect to the O'Brien Premises was completed and the related contingencies satisfied. As a result, we recorded \$23.0 million in "Gain on lease amendments" in the consolidated statements of operations and comprehensive loss for the year ended December 31, 2015, reflecting that our rent payments were reduced to zero for the remaining term of our existing Menlo Park facility real property leases, the aggregate of \$20.0 million in Landlord Payments became receivable and any associated financing obligation was revalued. Of the \$20.0 million in Landlord Payments, the first \$5.0 million Landlord Payment was received in September 2015, \$10.0 million was recorded as a short term receivable in "Prepaid and Other Current Assets" and the final \$5.0 million was recorded in "Other Long-term Assets" as of December 31, 2015. We do not believe that there are any remaining performance obligations relating to the remaining Landlord Payments. Subsequently, during February 2016 we received the second \$5.0 million Landlord payment.

O'Brien Lease Agreement

On July 22, 2015, we entered into the O'Brien Lease with respect to the O'Brien Premises. The term of the O'Brien Lease is one hundred thirty-two (132) months, commencing on the date that is the later of April 15, 2016 or the date on which the O'Brien Premises landlord has substantially completed certain shell improvements and tenant improvements. However, if any delay in the construction schedule is attributable to us under the lease, the lease will commence on the date substantial completion would have occurred but for the delay. Based on the currently agreed construction schedule, the O'Brien Lease will commence no earlier than June 15, 2016 and we believe that substantial completion will occur no earlier than August 1, 2016. Base monthly rent shall be abated for the first six (6) months of the lease term and thereafter will be \$540,000 per month during the first year of the lease term, with specified annual increases thereafter until reaching \$711,000 per month during the last twelve (12) months of the lease term. We were required to pay \$2,160,000 in prepaid rent which will be applied to the monthly rent installments due for the first to fourth months after the rent abatement period. We are also required to prepay \$180,000 (or the landlord's then-current estimate) in operating expenses for the first month of the lease term no later than March 15, 2016. We were also required to establish a deposit of \$4.5 million in the form of a letter of credit in October 2015; and as such, \$4.5 million was recorded in "Long-term restricted cash" in the consolidated balance sheet as of December 31, 2015. The landlord is obligated to construct certain shell improvements at the landlord's cost and expense and provide us with improvement allowances in the amount of \$12.6 million.

Under the O'Brien Lease, we expect to pay approximately \$80 million in rent and \$24 million in operating expenses over the expected lease term. In addition to the lease payments, we are also required to reimburse the landlord for certain improvement costs in excess of the tenant improvement allowances provided. These improvement costs, along

with the costs associated with the anticipated move to the O'Brien Premises, are expected to be substantial in nature. These future expenditures are expected to be partially offset by the \$15.0 million of future Landlord Payments from our Existing Landlord as described above.

The following table provides summary information concerning our contractual obligations as of December 31, 2015.

	Payments due by period (in thousands)					
	Total	2016	2017	2018	2019	2020
Operating lease obligations (1)	\$ 389	\$ 131	\$ 146	112	\$ —	\$ —
Debt (2)	27,184	1,799	1,794	5,632	2,817	15,142
Total contractual obligations	\$ 27,573	\$ 1,930	\$ 1,940	\$ 5,744	\$ 2,817	\$ 15,142

(1) Not including the O'Brien Lease described above due to uncertainty associated with the timing and completion of landlord improvements. Additionally, maintenance, insurance, taxes and contingent rent obligations are excluded. See "Note 7. Commitments and contingencies" in Part II, Item 8 of this Form 10-K for additional information.

(2) Under the terms of the Facility Agreement and the Notes, we received \$20.5 million in funding. The amounts in the table above include interest and principal repayments on the debt.

Other Purchase Commitments

In addition (and not included in the table above), we have other purchase commitments of an estimated amount of approximately \$14.4 million consisting of 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, and acquisition and licensing of intellectual property. 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.

Off-Balance Sheet Arrangements

As of December 31, 2015 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 7. 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, 2015.

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, 2015 would have resulted in a \$0.5 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.

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, 2015 and 2014, 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, 2015. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements 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, 2015 and 2014, and the consolidated results of its operations, and its cash flows for each of the three years in the period ended December 31, 2015, in conformity with U.S. generally accepted accounting principles.

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, 2015, 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 11, 2016 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

Redwood City, California

March 11, 2016

PACIFIC BIOSCIENCES OF CALIFORNIA, INC.

Consolidated Balance Sheets

(in thousands, except per share amounts)	December 31,	
	2015	2014
Assets		
Current assets		
Cash and cash equivalents	\$ 33,629	\$ 36,449
Investments	48,641	64,899
Accounts receivable	5,245	3,406
Inventory	10,955	11,335
Prepaid expenses and other current assets	12,071	1,671
Total current assets	110,541	117,760
Property and equipment, net	8,548	6,601
Long-term restricted cash	4,500	—
Other long-term assets	7,518	29
Total assets	\$ 131,107	\$ 124,390
Liabilities and Stockholders' Equity		
Current liabilities		
Accounts payable	\$ 4,749	\$ 5,608
Accrued expenses	15,551	11,441
Deferred service revenue, current	6,815	6,121
Deferred contractual revenue, current	10,822	6,785
Other liabilities, current	241	1,534
Total current liabilities	38,178	31,489
Deferred service revenue, non-current	1,143	1,129
Deferred contractual revenue, non-current	1,312	19,735
Other liabilities, non-current	1,386	2,153
Notes payable	14,948	13,991
Financing derivative	600	944
Total liabilities	57,567	69,441
Commitments and contingencies (Note 7)		
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 79,983 and 73,927 shares at December 31, 2015 and 2014, respectively	80	74
Additional paid-in-capital	786,636	736,339
Accumulated other comprehensive income (loss)	(7)	9

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Accumulated deficit	(713,169)	(681,473)
Total stockholders' equity	73,540	54,949
Total liabilities and stockholders' equity	\$ 131,107	\$ 124,390

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,		
	2015	2014	2013
Revenue:			
Product revenue	\$ 37,502	\$ 35,299	\$ 20,039
Service and other revenue	10,896	8,511	6,446
Contractual revenue	44,384	16,784	1,696
Total revenue	92,782	60,594	28,181
Cost of Revenue:			
Cost of product revenue	30,704	29,626	15,706
Cost of service and other revenue	8,628	7,566	6,056
Total cost of revenue	39,332	37,192	21,762
Gross profit	53,450	23,402	6,419
Operating Expense:			
Research and development	60,440	48,230	45,217
Sales, general and administrative	45,187	38,026	38,745
Gain on lease amendments	(23,043)	—	—
Total operating expense	82,584	86,256	83,962
Operating loss	(29,134)	(62,854)	(77,543)
Interest expense	(2,926)	(2,828)	(2,478)
Other income (expense), net	364	(478)	728
Net loss	(31,696)	(66,160)	(79,293)
Other comprehensive loss:			
Unrealized loss on investments	(16)	(5)	(16)
Comprehensive loss	\$ (31,712)	\$ (66,165)	\$ (79,309)
Net loss per share:			
Basic and diluted net loss per share	\$ (0.42)	\$ (0.94)	\$ (1.26)
Shares used in computing basic and diluted net loss per share	75,614	70,475	62,784

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, 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" 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" 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
Net loss	—	—	—	—	(31,696)	(31,696)
Other comprehensive loss	—	—	—	(16)	—	(16)
Issuance of common stock in conjunction with equity plans	1,981	2	7,361	—	—	7,363
Issuance of common stock in conjunction with "at-the-market" offering, net of issuance costs	4,075	4	29,096	—	—	29,100
Stock-based compensation expense	—	—	13,840	—	—	13,840
Balance at December 31, 2015	79,983	\$ 80	\$ 786,636	\$ (7)	\$ (713,169)	\$ 73,540

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,		
	2015	2014	2013
Cash flows from operating activities			
Net loss	\$ (31,696)	\$ (66,160)	\$ (79,293)
Adjustments to reconcile net loss to net cash used in operating activities			
Depreciation and amortization	3,677	4,221	5,648
Amortization of debt discount and financing costs	957	793	595
Stock-based compensation	13,840	9,943	9,905
Non-cash portion of gain on lease amendments	(3,043)	—	—
Other items	(230)	507	(352)
Changes in assets and liabilities			
Accounts receivable	(1,738)	(660)	76
Inventory	(2,466)	(1,285)	(60)
Prepaid expenses and other assets	(17,889)	(224)	840
Accounts payable	(716)	3,891	(1,271)
Accrued expenses	5,732	3,536	1,327
Deferred service revenue	708	2,686	386
Deferred contractual revenue	(14,386)	(6,784)	33,304
Other liabilities	(639)	(1,932)	(938)
Net cash used in operating activities	(47,889)	(51,468)	(29,833)
Cash flows from investing activities			
Purchase of property and equipment	(3,009)	(1,609)	(909)
Proceeds from disposal of property and equipment	36	—	—
Long-term restricted cash	(4,500)	—	—
Purchase of investments	(84,579)	(126,413)	(201,547)
Sales of investments	8,317	—	100
Maturities of investments	92,341	147,586	169,239
Net cash provided by (used in) investing activities	8,606	19,564	(33,117)
Cash flows from financing activities			
Proceeds from issuance of common stock from equity plans	7,363	3,968	3,079
Proceeds from issuance of common stock from "at-the-market" offering, net of issuance costs	29,100	38,023	19,927
Proceeds from issuance of debt agreement, net of issuance costs	—	—	19,766
Net cash provided by financing activities	36,463	41,991	42,772
Net increase (decrease) in cash and cash equivalents	(2,820)	10,087	(20,178)
Cash and cash equivalents at beginning of period	36,449	26,362	46,540
Cash and cash equivalents at end of period	\$ 33,629	\$ 36,449	\$ 26,362

Supplemental disclosure of cash flow information

Interest paid	\$ 1,794	\$ 1,794	\$ 1,165
Supplemental disclosure of non-cash investing and financing activities			
Inventory transferred to (from) property and equipment	2,846	—	(558)

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

We design, develop and manufacture sequencing systems to help scientists resolve genetically complex problems. Based on our novel Single Molecule, Real-Time (SMRT®) Sequencing 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.

In September 2015, we announced that we had launched a new nucleic acid sequencing platform, the PacBio Sequel™ System (the “Sequel System”), which will provide higher throughput, more scalability, a reduced footprint and lower sequencing project costs compared to the PacBio® RS II System, while maintaining the existing benefits of our SMRT Technology.

The names “Pacific Biosciences,” “PacBio,” “SMRT,” “SMRTbell,” “Sequel” 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 U.S. 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 U.S. GAAP requires us to make estimates and assumptions that affect the amounts reported in the financial statements and accompanying notes to the financial statements. Our estimates include, but are not limited to, the valuation of inventory, revenue valuation, the valuation of a financing derivative and long-term notes, the valuation and recognition of share-based compensation, 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.

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 included four quarterly periods of amortization of \$1.7 million from the non-refundable up-front payment of \$35.0 million. During the first quarter of 2015, we revised the estimated period over which the delivery of elements pursuant to the Roche Agreement is expected to occur, due to an increased level of certainty regarding the development period. As a result, we are, on a prospective basis, recognizing the remaining deferred contractual revenue associated with the upfront payment received under the Roche Agreement over the revised estimated remaining development period. For the year ended December 31, 2015, this change in estimate increased contractual revenue by \$7.6 million, and decreased our basic and diluted net loss per share by \$0.10 per share.

Fair Value of Financial Instruments

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

The fair value hierarchy established under U.S. 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, 2015 and 2014, respectively (in thousands):

(in thousands)	December 31, 2015				December 31, 2014			
	Level 1	Level 2	Level 3	Total	Level 1	Level 2	Level 3	Total
Assets								
Cash and cash equivalents:								
Cash and money market funds	\$ 22,034	\$ —	\$ —	\$ 22,034	\$ 21,952	\$ —	\$ —	\$ 21,952
Commercial paper	—	8,595	—	8,595	—	14,497	—	14,497
US government & agency securities	—	3,000	—	3,000	—	—	—	—
Total cash and cash equivalents	22,034	11,595	—	33,629	21,952	14,497	—	36,449
Investments:								
Commercial paper	—	15,903	—	15,903	—	43,653	—	—