PACIFIC BIOSCIENCES OF CALIFORNIA, INC.
Form 10-K
March 14, 2014

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, 2013

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	16-1590339
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)

1380 Willow Road

Menlo Park, CA 94025 (Address of principal executive offices) 94025 (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, 2013, based upon the closing price of Common Stock on such date as reported by NASDAQ Global Select Market, was approximately $124,086,000. 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 10, 2014: 70,458,497

DOCUMENTS INCORPORATED BY REFERENCE:

Portions of the registrant's definitive Proxy Statement relating to its 2014 Annual Meeting of Stockholders to be held on May 22, 2014 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

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 our management’s beliefs and assumptions and on information currently available to our management. The statements contained in this Annual Report on Form 10-K that are not purely historical are forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended (the “Exchange Act”), and include, but are not limited to our statements regarding the sequencing advantages of SMRT technology, market opportunities, strategic plans, expectations regarding the conversion of backlog to revenue, expectations regarding our collaboration agreements including expected revenue and related milestone payments, manufacturing plans, research and development plans, 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. Such statements may be signified by terms such as “anticipates,” “believes,” “could,” “seeks,” “estimates,” “expects,” “intends,” “may,” “plans,” “po “predicts,” “projects,” “should,” “will,” “would” or similar expressions and the negatives of those terms. Forward-looking statements involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. Factors that could cause or contribute to such differences include, but are not limited to, those discussed under the heading “Risk Factors” in this report and in other documents we file with the Securities and Exchange Commission (“SEC”). Given these risks and uncertainties, you should not place undue reliance on forward-looking statements. Also, forward-looking statements represent management’s beliefs and assumptions as of the date of this report. 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.

PART I

ITEM 1.BUSINESS

Overview

We develop, manufacture and market an integrated platform for high resolution genetic analysis. We have developed a technology to study the synthesis, composition, structure, and regulation of DNA. Combining advances in nanofabrication, biochemistry, molecular biology, surface chemistry and optics, we created a technology platform using our proprietary single molecule, real-time, or SMRT, technology. Our SMRT technology uses the natural processing power of enzymes, combined with specially designed reagents and detection systems, to record individual biochemical events as they occur. The ability to observe single molecule events in real time provides the scientific community with an advanced tool for investigating basic biochemical processes such as DNA synthesis. Our SMRT technology has the potential to advance scientific understanding by providing a window into biological processes that has not previously been open.

Our initial focus is to offer our SMRT technology to the DNA sequencing market where we have developed a third generation sequencing platform, the PacBio RS II sequencing system. The PacBio RS II is an instrument that uses our proprietary consumables, including our SMRT Cells and reagent kits that are used to prepare and sequence DNA samples.

The PacBio RS II maintains many of the key attributes of first and second generation sequencing technologies while solving many of their inherent limitations, including short read lengths, limited flexibility, long time to result, complex sample preparation and risk of amplification bias. Our system provides long read lengths, flexibility in experimental design, fast time to result, and avoidance of amplification bias. Our system is designed to be integrated into existing laboratory workflows and information systems.

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

The Underlying Science

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

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

DNA as a template to synthesize new strands of messenger RNA, or mRNA. The mRNAs are then translated into proteins by ribosomes. The resulting proteins go on to play crucial roles in cellular structure and function and thus the operation of biological systems.

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

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

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

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

oxoguanine and many others, play important physiological roles. In bacteria, 6-methyladenine has been shown to play an important role in pathogenicity.

In a published study in Nature Biotechnology of a Shiga-toxin-producing E. coli strain that caused a serious outbreak in northern Germany in 2011 that killed approximately 50 people and sickened over 1,000 others, researchers had previously sequenced the genome of the same strain; however, the data had not explained the high virulence of the strain. By analyzing the outbreak strain sequence for 6-methyladenine residues using our first commercial product, the PacBio RS, researchers discovered a series of methylase-like enzymes that targeted specific sequences throughout the genome as they made their chemical changes. Follow-up studies of a particular methylase suggest that it alters the expression of gene pathways related to horizontal gene transfer — an important property that could be linked to virulence.

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

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

Evolution of Sequencing

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

First Generation Sequencing

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

Second Generation Sequencing

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

In most second generation tools, tens of thousands of identical strands are anchored to a given location to be read in a process consisting of successive flushing and scanning operations. The “flush and scan” sequencing process involves sequentially flushing in reagents, such as labeled nucleotides, incorporating nucleotides into the DNA strands, stopping the incorporation reaction, washing out the excess reagent, scanning to identify the incorporated base and finally treating that base so that the strand is ready for the next “flush and scan” cycle. This cycle is repeated until the reaction is no longer viable.

Due to the large number of flushing, scanning and washing cycles required, the time to result for second generation methods is generally long, often taking days. This repetitive process also limits the average read length produced by most second generation systems under standard sequencing conditions to approximately 35 to 400 bases. The array of DNA anchor locations can have a high density of DNA fragments, leading to extremely high overall throughput and a resultant low cost per identified base when the machine is run at high capacity. However, the disadvantages of second generation sequencing include short read length, complex sample

preparation, the need for amplification, long time to result, the need for many samples to justify machine operation and significant data storage and interpretation requirements.

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

Pacific Biosciences' Solution — The Third Generation of Sequencing Technology

We have developed a technology platform that enables single molecule, real-time, or SMRT, detection of biological processes. Based on our SMRT technology platform, we have introduced a third generation DNA sequencing system, the PacBio RS II, that addresses many of the limitations of the first and second generation technologies, by providing longer read lengths, increased flexibility, reduced time to result, simplified sample preparation and elimination of amplification bias. In addition, the PacBio RS II enables the study of modified bases through its unique feature of detecting the kinetics of base incorporation during DNA synthesis.

Pacific Biosciences' SMRT Technology

Our 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 that is 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 observing the natural activity of the DNA polymerase, an enzyme that is 15 nanometers (nm) in diameter running in real time, we introduced three key innovations:

•The SMRT Cell

•Phospholinked nucleotides

•The PacBio RS II

The SMRT Cell

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

A ZMW is a hole, tens of nanometers in diameter. The small size of the ZMW prevents visible laser light, which has a wavelength of approximately 600nm, from passing entirely through the ZMW. Rather than passing through, the light decays as it enters the ZMW. Therefore, by shining a laser into the ZMW, only the bottom 30nm of the ZMW becomes illuminated. DNA polymerases are anchored to the bottom of the glass surface of the ZMWs using a proprietary technique. Nucleotides, each type labeled with a different colored fluorophore, are then flooded above an array of ZMWs at the required concentration. As no laser light penetrates up through the holes to excite the fluorescent labels, the labeled nucleotides above the ZMWs do not fluoresce. Only when they diffuse into the bottom 30nm of the ZMW do they fluoresce. When the correct nucleotide is detected by the polymerase, it is incorporated into the growing DNA strand in a process that takes milliseconds in contrast to simple diffusion which takes

microseconds. This difference in time results in higher signal intensity for incorporated versus unincorporated nucleotides, which creates a high signal-to-noise ratio. Thus, the ZMW has the ability to detect a single incorporation event against the background of fluorescently labeled nucleotides at biologically relevant concentrations. Our DNA sequencing is performed on proprietary SMRT Cells, each having an array of approximately 150,000 ZMWs. Each ZMW is capable of containing a DNA polymerase molecule bound to a single DNA template. Currently, our immobilization process randomly distributes polymerases into ZMWs across the SMRT Cell, resulting in approximately one-third of the ZMWs being available for use.

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 completely natural piece of DNA with no evidence of labeling remaining.

The PacBio RS II

The PacBio RS II is an instrument that conducts, monitors, and analyzes single molecule biochemical reactions in real time. The PacBio RS II uses a high numerical aperture objective lens and four single-photon sensitive cameras to collect the light pulses emitted by fluorescent reagents allowing the observation of biological processes. An optimized set of algorithms is used to translate the information that is captured by the optics system. Using the recorded information, light pulses are converted into either an A, C, G or

T base call with associated quality metrics. Once sequencing is started, the real-time data is delivered to the system's primary analysis pipeline, which outputs base identity and quality values, or QVs. To generate a consensus sequence from the data, an assembly process aligns the different fragments from each ZMW based on common sequences.

SMRT Sequencing Advantages

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

•Single molecule, real-time analysis. The ability to observe single molecules in real time combined with long read length allows our system to observe structural and cell type variation that present challenges for existing short-read technologies. Unlike many other sequencing platforms, minimal amounts of reagent and sample preparation are required and there are no time-consuming flushing, scanning and washing steps.

•Longer read lengths. Our SMRT technology has been demonstrated to produce a distribution of read lengths of over 8,500 base pairs on average, with the longest read lengths in excess of 40,000 base pairs, which facilitates mapping and assembly. Longer read lengths require the sequencing of fewer overlapping segments, referred to as coverage, to efficiently assemble the underlying genomic structure. 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 large-scale rearrangements observed in cancer. Long read lengths are also highly enabling for de novo assembly of genomes, where reference genomes do not exist or are not used for the assembly.

•More uniformity and less systematic error. The sample preparation step for SMRT sequencing does not require amplification and therefore the reads are not subject to amplification bias. Importantly, this allows for uniform identification of all bases present in a DNA sample. As a result, SMRT sequencing can detect and identify regions and entire genes that may be missed by second generation sequencing technologies. In addition, the read errors from SMRT sequencing are largely random, and therefore they can be more easily resolved by aligning and comparing multiple overlapping reads. Second generation sequencing technologies generally have more systematic read errors, and are more difficult to resolve because identical errors are more likely to be present in each overlapping read. As a result, we believe that SMRT sequencing can enable a more complete assembly of genomes and higher consensus accuracy with less coverage than other available sequencing technologies.

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

•Faster time to result. With the PacBio RS II, sample preparation to sequencing results can take less than one day. A typical sequencing run can require as little as 30 to 180 minutes of instrument time, with target polymerase speeds of two to three bases per second, compared to other technologies which can take multiple days to produce results. This

fast time to result may have important implications for applications where speed is of critical importance such as infectious disease monitoring and molecular pathology.

•Flexibility and granularity. The PacBio RS II system offers multiple protocols, including standard and circular consensus sequencing, enabling the user to optimize performance based on the needs for a particular project. It can be used with a variety of sample types and can output a range of DNA lengths. The system also has the ability to scale the throughput and cost of sequencing across a range of small and large projects.

•Ability to observe and capture kinetic information. The ability to observe the activity of a DNA polymerase in real time enables the PacBio RS II to collect, measure and assess the dynamics and timing of nucleotides being added to a growing DNA strand, referred to as kinetics. It is well established in the scientific community that chemical modification of DNA such as the addition of a methyl group, known as methylation, can alter the biological activity of the affected nucleotide. The PacBio RS II detects changes in kinetics automatically by capturing and recording changes in the duration of, and distances between, each of the fluorescent pulses during a typical sequencing analysis. Integrated software can then translate these kinetic signatures into uniquely characterized modified bases such as 6mA, 4mC and 5mC in bacteria. First and second generation sequencing systems are unable to accurately record this type of kinetic data because the “flush and scan” sequencing process disrupts the timing of the natural incorporation process and the amplification step during sample preparation erases these modifications in the first place.

•Ease of use. Our system is designed to be easy to use and adopt because it is compatible with existing lab workflows and informatics infrastructures. Our SMRTbell sample preparation protocol is designed to be simple and fast. The PacBio RS

II is equipped with a touchscreen interface that requires minimal user intervention. The data format has been designed to be compatible with standard informatics systems. We believe that these attributes allow for easy training at customer sites.

Our Products

We entered the market with our first commercial product, the PacBio RS, and more recently launched the PacBio RS II, which are third generation sequencing instruments that provide real-time information at the single molecule level. The initial application for the system is DNA sequencing, and the architectural design of the system may enable a broader range of applications over time. The instrument is designed for expandable capability to permit performance improvements and new applications to be delivered through chemistry and software enhancements without necessitating changes to the hardware.

Our sequencing system includes the PacBio RS II instrument platform that uses our proprietary consumables, including our SMRT Cells and reagent kits, providing a complete solution to the customer.

The PacBio RS II

The PacBio RS II is an instrument that conducts, monitors and analyzes biochemical sequencing reactions. The instrument is an integrated unit that includes high performance optics, automated liquid handling, a touchscreen control interface, a computational Blade Center and software. The instrument's high performance optics monitor the thousands of ZMWs in real time. The automated liquid handling system performs reagent mixing and prepares SMRT Cells. The instrument's touchscreen control interface, the RS Touch, is the user's primary control center to design and monitor experiments as they occur in real time. The Blade Center is the computational brain of the PacBio RS II, responsible for processing the sequencing data being produced on the SMRT Cells. The PacBio RS II has been designed to allow for performance improvements without replacement of the instrument hardware.

Consumables

To run our PacBio RS II, our customers must purchase our proprietary consumable products. Our consumable products include our proprietary SMRT Cells and reagent kits. One SMRT Cell is consumed per sequencing reaction on the PacBio RS II. Eight SMRT Cells are individually hermetically sealed and packaged together into a streamlined 8Pac format. This enables a researcher to use one or more SMRT Cells per run.

We offer several reagent kits, each designed to address a specific step in the workflow. The Template Preparation Kit is used to convert DNA into our SMRTbell double-stranded DNA library format and therefore includes typical molecular biology reagents, such as ligase, buffers and exonucleases. The Binding Kit, which includes our modified DNA polymerase, is then used to bind this library to the polymerase in preparation for sequencing. The Sequencing Kit contains the reagents required for on-instrument, real-time sequencing, including the phospholinked nucleotides. Each sample can be sequenced in a single SMRT Cell or across many SMRT Cells depending on the needs of the project. As a result, the price per reaction is dependent on the experiment design.

Product Enhancements

During 2013, we introduced a number of product enhancements that improved the performance and reliability of our products. In the first quarter of 2013, we introduced a software upgrade which included a highly enabling method for de novo genome assembly called HGAP and a consensus algorithm called Quiver. Together, these software tools greatly simplified the process for users to analyze data generated by their PacBio instruments and to assemble highly accurate genomes using only standard, PacBio long reads. During the second quarter, we introduced the PacBio RS II

system and RS to RS II upgrade kit, which effectively doubled the throughput of the original PacBio RS. In the fourth quarter, we introduced our P5 polymerase and C3 chemistry combination (P5-C3), which enables customers to generate sequences with read lengths averaging over 8,500 bases, with the longest read lengths exceeding 40,000 bases. This chemistry release along with associated software enables customers to nearly double the throughput previously generated from each SMRT Cell.

During 2014 and beyond we plan to further leverage our SMRT technology and existing PacBio RS and RS II instruments by introducing additional consumable product enhancements that will improve read lengths and throughput. In addition, we have partnered with F. Hoffman- La Roche Ltd. ("Roche") to explore and develop SMRT technology-based products for diagnostic applications.

Market for Our Products

Our customers use our products for sequencing the genomes of a wide range of organisms. With its current throughput capability, the PacBio RS II is well-suited for sequencing small and medium size genomes, such as bacteria and fungi, and for sequencing targeted regions of larger genomes such as humans and plants. Over the past year, we have increased the throughput of the PacBio RS II through product enhancements, which we believe expands the targeted applications for our products. We plan on continuing to increase throughput with future product enhancements.

There are a number of emerging markets for sequencing-based tests, including molecular diagnostics, which represent significant potential opportunities for our products. The development of these markets is subject to variability driven by ongoing changes in the competitive landscape, evolving regulatory requirements, government funding of research and development activities,

and macroeconomic conditions. Introductions of new technologies and products, while positive to the overall development of these markets, may result in greater competition for the limited financial resources available. As we continue to expand into these emerging markets, the development of our business will be impacted by the variability of the factors affecting the growth of these markets.

Pacific Biosciences' Strategy

We plan to execute the following strategy:

•Contribute to the future of biological analysis by offering 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, complete assemblies, and short time to result afford the scientific community a new tool to conduct research not possible with first and second generation sequencing instruments.

•Focus initially on a small number of sequencing applications in which our SMRT technology provides unique capability. While we believe our third generation sequencing technology will address many of the limitations of other sequencing technologies and enable a wide range of experiments and applications, we plan to drive adoption of our technology by focusing initially on applications that our customers have identified as high-value applications for SMRT sequencing. Among the early applications identified by our customers are de novo Genome Assembly, Targeted Sequencing and Base Modification 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.

•Continually enhance product performance to increase market share. The design of the PacBio RS II allows for significant performance improvements without replacement of the instrument hardware. Our flexible platform is designed to generate a recurring revenue stream through the sale of proprietary SMRT Cells and reagent kits. Our research and development efforts are focused on product enhancements to reduce DNA sequencing cost and time as well as expand capabilities. During 2013 we introduced the PacBio RS II System, our P5-C3 chemistry, and significant enhancements to our software analysis toolkit. These product enhancements have enabled an approximate 2x improvement in read length and an approximate 4x improvement in throughput per SMRT Cell. In addition, the software analysis tools have improved the ease of use of our products and have enabled our customers to take greater advantage of their SMRT sequencing data. We plan to continue introducing enhancements to our products over time.

•Leverage our technology to develop and launch additional applications. We plan to leverage our SMRT technology platform to develop new applications such as sequencing larger and more complex genomes and expanding the ability to detect and characterize base modifications. In 2013, we entered into a collaboration agreement with Roche to jointly develop products based on our SMRT technology for the human in vitro diagnostics market. In the long term, our SMRT technology may also be adapted for RNA transcription monitoring, direct RNA sequencing, protein translation and ligand binding. We believe these applications can create substantial new markets for our technology.

•Create a global community of users to enhance informatics capabilities and drive adoption of our products. We have worked closely with members of the informatics community to develop and define standards for working with single molecule, real-time sequence data. We maintain the PacBio DevNet site, a website on which we make available various software tools and information about our SMRT sequencing technology to support academic informatics developers, life scientists and independent software vendors interested in creating tools to work with our third generation sequencing data. This gives the user flexibility to perform further analysis of the sequencing data through third-party software or share data with collaborators. To maximize the flexibility and functionality for all users, all of our secondary analysis algorithms are made available under an open source license. We also maintain the PacBio SampleNet site, a website on which we make available various tools for simplifying and enhancing sample preparation protocols.

Marketing, Sales, Service and Support

We market our products through a direct sales force in North America and Europe and primarily through distributors in Asia. Our sales strategy involves the use of a combination of sales managers, sales representatives and field application specialists. The role of our sales managers and sales representatives is to educate customers on the advantages of SMRT technology and the applications that our technology makes possible. The role of our field application specialists is to provide on-site training and scientific technical support to prospective and existing customers. Our field application specialists 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 our field service engineers. Our 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 specialists. 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 genome centers, clinical, government and academic institutions, genomics service providers, pharmaceutical companies and agricultural companies. In general, our customers will isolate, prepare and analyze genetic samples using the PacBio RS and PacBio RS II 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 each of the years ended December 31, 2013, 2012 and 2011, no single end customer accounted for more than 10% of our total revenue.

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

We currently sell our products to a number of customers outside the United States, including customers in other areas of North America, Europe, and Asia. Revenue from customers outside the United States totaled $14.6 million, or 52% of our total revenue, during fiscal 2013, compared to $14.6 million, or 56%, in fiscal 2012, and $6.3 million, or 19%, in fiscal 2011. See also “Note 12. Segment and Geographic Information” in the Notes to Consolidated Financial Statements of this Form 10-K.

Backlog

As of December 31, 2013, our system revenue backlog was approximately $7.4 million, compared to $2.9 million at December 31, 2012. 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 2014 subject to customers who may otherwise seek to cancel or delay their orders even if we are prepared to fulfill them.

Manufacturing

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

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

Research and Development

Our SMRT technology requires the blending of a number of unique disciplines, namely nanofabrication, physics, photonics, optics, molecular biology, engineering, signal processing, high performance computing, and bioinformatics. Our research and development team is a blend of these disciplines creating a single, cross-functional operational unit. We have also established productive working relationships with technology industry leaders, as well as leading academic centers, to augment and complement our internal research and development efforts. Research and development expense incurred was $45.2 million, $47.6 million and $76.1 million during 2013, 2012 and 2011, respectively. We plan to continue investment in research and development to enhance the performance and expand the application of our current products, and introduce additional products based on our SMRT technology. Our goals include further improvements in sequencing read length and mappable data per SMRT Cell, chemistry and software enhancements for expanding base modification analysis, and enhancements in sample preparation and bioinformatics tools that take advantage of the capabilities of our products. In addition, our engineering teams will continue their focus on increasing instrument component and system reliability, reducing costs, and implementing additional system flexibility and versatility through the enhancement of existing products and development of new products.

Intellectual Property

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

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

As of December 31, 2013, we own or hold exclusive licenses to 134 issued U.S. patents, 114 pending U.S. patent applications, 65 granted foreign patents and 107 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 2032. We also have non-exclusive patent licenses with various third parties to supplement our own large and robust patent portfolio.

Of these patents and patent applications, 22 issued U.S. patents, three pending U.S. patent applications, 19 granted foreign patent and four pending foreign patent applications are licensed to us by the Cornell Research Foundation, which manages technology transfers on behalf of Cornell University, collectively referred to as Cornell. We have also entered into a license agreement with Indiana University Research and Technology Corporation, or IURTC, for U.S. Patent No. 6,399,335, which relates to nucleoside triphosphates that include a labeling group attached through the terminal phosphate group in the triphosphate chain. We have also entered into a license agreement with GE Healthcare Bio-Sciences Corp, or GE Healthcare, for several U.S. and foreign patents and pending patent applications related to labeled nucleoside polyphosphate compounds.

In September 2013, we entered into a Development, Commercialization and License Agreement (the “Roche Agreement”) with Roche, pursuant to which we: (i) will develop diagnostic products for clinical use including sequencing systems and consumables based on our proprietary SMRT technology; (ii) granted to Roche an exclusive right to commercialize, and an exclusive license to sell, the developed diagnostic products for clinical use; and (iii) will manufacture and supply certain products intended for clinical use as the exclusive supplier to Roche. We received a non-refundable up-front payment of $35.0 million and may receive up to an additional $40.0 million based upon the achievement of development milestones. The Roche Agreement has an initial term of thirteen years and provisions allowing Roche 5-year renewals.

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

Competition

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

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

Employees

As of December 31, 2013, we had 318 full-time employees. Of these employees, 120 were in research and development, 58 were in operations, 97 were in marketing, sales, service and support, and 43 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 web site is located at www.pacb.com. The information posted on our web site 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 web site as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC.

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, the PacBio RS, launched in 2011 and our most recent product, the PacBio RS II, launched in 2013 and, as such, we have limited historical financial data upon which to base our projected revenue, planned operating expense or upon which to evaluate us and our commercial prospects. Based on our limited experience in developing and marketing new products, we may not be able to effectively:

•drive adoption of our products;

•attract and retain customers for our products;

•provide appropriate levels of customer training and support for our products;

•implement an effective marketing strategy to promote awareness of our products;

•focus our research and development efforts in areas that generate returns on these efforts;

•comply with evolving 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 products;

•scale our manufacturing activities to meet potential demand at a reasonable cost;

•avoid infringement and misappropriation of third-party intellectual property;

•obtain licenses on commercially reasonable terms to third-party intellectual property;

•obtain valid and enforceable patents that give us a competitive advantage;

•protect our proprietary technology;

•protect our products from any equipment or software-related system failures; and

•attract, retain and motivate qualified personnel.

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

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

We have incurred net losses since inception and we cannot be certain if or when we will produce sufficient revenue from our operations to support our costs. Even if profitability is achieved, we may not be able to sustain profitability. We expect to incur substantial losses and negative cash flow 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 practical with other current technologies. To accomplish this, we must successfully commercialize, and continue development of, our SMRT technology for use in a variety of life science applications. There can be no assurance that we will be successful in securing additional customers for our products. Furthermore, we cannot guarantee that the design, performance or specifications of our products will be satisfactory to potential customers in the markets we seek to reach. These markets are dynamic, and there can be no assurance that they will develop as quickly as we expect or that they will reach their full potential. As a result, we may be required to refocus our marketing efforts, and we may have to make changes to the specifications of our products to enhance our ability to enter particular markets more quickly. Even if we are able to implement our technology successfully, we may fail to achieve or sustain market acceptance of our products by academic and government research laboratories and pharmaceutical, biotechnology and agriculture companies, among others, across the full range of our intended life science applications. If the market for our products

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

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

We have entered into an agreement with Roche, pursuant to which we will develop and manufacture diagnostic products for clinical use including sequencing systems and consumables based on our proprietary Single Molecule, Real-Time (SMRT®) technology. There can be no assurance that we will be able to develop and manufacture products as provided by the terms of the Roche Agreement or that Roche will be able to commercialize and sell the developed diagnostic products. We may also be unable to meet the development milestones required for additional payments from Roche. We could also be involved in disputes with Roche, which could lead to delays in or termination of our development and manufacture of diagnostic products and result in time consuming and expensive litigation or arbitration. In addition, any such dispute could diminish Roche's commitment to us and reduce the resources they devote to commercializing the developed diagnostic products. If Roche terminates or breaches the Roche Agreement, or otherwise acquires, develops and/or commercializes alternative or competing products, the successful commercialization of our diagnostic products for clinical use would be materially and adversely affected. If we are not able to realize the expected benefits from the Roche Agreement, it could have a material adverse effect on our business, financial condition and results of operations.

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

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

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

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

We have entered into a debt agreement, pursuant to which we received $20.5 million in funding. Our net losses since inception and our expectation of incurring substantial losses and negative cash flow for the foreseeable future, combined with indebtedness could:

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

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

Our debt agreement contains various affirmative and negative covenants, including restrictions on our and our subsidiaries' ability to incur additional indebtedness or liens on our assets, except as permitted under the debt agreement, that impose significant operating and financial restrictions on us, including restrictions on our ability to take actions that may be in our best interests, some of which may be affected by events beyond our control.

A breach of any of the covenants contained in our debt agreement could result in a default under such agreement. If an event of default exists, debt holders could elect to declare all amounts outstanding under the debt agreement 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 intellectual property, as collateral under the debt agreement. If the debt holders accelerate the repayment of borrowings, we may not have sufficient funds to repay our existing indebtedness, which could have a material adverse effect on our liquidity and ability to conduct our business.

Our products are highly complex and have recurring support requirements.

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

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

In order to successfully derive revenue from our products, we need to supply our customers with products that meet the specifications, quality requirements and expectations of our customers. Our customers have previously experienced variability in the performance of our instruments and SMRT Cells. There is no assurance that we will be able to manufacture our products so that they consistently achieve the product specifications and quality that our customers expect, including those products and specification developed pursuant to the Roche Agreement. There is also no assurance that we will be able to increase manufacturing yields and decrease costs. Furthermore, we may not be able to increase manufacturing to meet anticipated demand. An inability to manufacture products that consistently meet specifications, in necessary quantities and at commercially acceptable costs, will have a negative material impact on our business.

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

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

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

Our instrument sales represent significant capital purchases for our customers. Our potential customers include academic and government institutions, genome centers, medical research institutions, pharmaceutical, agricultural, biotechnology 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, particularly in light of the recent United States federal government shutdown, 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 be unable to successfully increase sales of our products.

Our ability to achieve profitability depends on our ability to attract customers for our 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 globally or in certain regions of the world. There is no guarantee, when we enter into such arrangements, that we will be successful in attracting desirable sales and distribution partners; there is also no guarantee that we will be able to enter into such arrangements on terms favorable to us. If our sales and marketing efforts, or those of any of our third-party sales and distribution partners, are not successful, our technologies and products may not gain market acceptance, which could materially impact our business operations.

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

Our products are complex and involve a large number of unique components, many of which require precision manufacturing. The nature of the products requires customized components that are currently available only from a limited number of sources, and in some cases, single sources. We have chosen to source certain critical components from a single source, including suppliers for our SMRT Cells, reagents and instruments. If we are required to purchase these components from an alternative source, it could take several months or longer to qualify the alternative sources. If we are unable to secure a sufficient supply of these product components, we will be unable to manufacture and sell our products in a timely fashion or in sufficient quantities or under acceptable terms. Additionally, for some of those components that are currently purchased from a sole or single source supplier, we have not yet arranged for alternative suppliers.

The operations of our third-party manufacturing partners and suppliers could be disrupted by conditions unrelated to our business or operations or beyond our control. If our manufacturing partners or suppliers are unable or fail to fulfill their obligations to us for any reason, we may not be able to manufacture our products and satisfy customer demand or our obligations under sales agreements in a timely manner, and our business could be harmed as a result. Our current manufacturing process is characterized by long lead times between the ordering and delivery of our products. If we 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.

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

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

personnel, including scientists, engineers and others, could prevent us from pursuing collaborations and adversely affect our product development and introductions, business growth prospects, results of operations and financial condition.

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

We have raised, and 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. We intend to raise additional funds beyond the transactions completed to date, which will result in additional dilution to our stockholders.

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, as well as many of our potential competitors, have greater name recognition, more substantial intellectual property portfolios, longer operating histories, significantly greater resources to invest in new technologies, more substantial experience in new product development and manufacturing capabilities and 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 accept competitive

products and services in lieu of purchasing our products. Increased competition may result in pricing pressures, which could harm our sales, profitability or market share. Our failure to compete effectively could materially and adversely affect our business, financial condition or results of operations.

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

Products using our SMRT technology are complex and may develop or contain undetected defects or errors. We cannot provide assurance that material performance problems will not arise. Despite testing, defects or errors may arise in our products, which could result in a failure to achieve increased market acceptance, diversion of development resources, injury to our reputation and increased warranty, service and maintenance costs. We ship our PacBio RS II 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, but claims must be made within 30 days from the shelf life date or "use by" date. The warranty is limited to replacing, or at our option, giving credit for, any consumable with defects in material or workmanship. Defects or errors in our products might also discourage customers from purchasing our products. The costs incurred in correcting any defects or errors may be substantial and could adversely affect our operating margins. In addition, such defects or errors could lead to the filing of product liability claims against us or against third parties who we may have an obligation to indemnify against such claims, which could be costly and time-consuming to defend and result in substantial damages. Although we have product liability insurance, any product liability insurance that we have or procure in the future may not protect our assets 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.

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 will be useful with our products or be viewed as useful by our customers or potential customers. A lack of additional available complementary sample preparation and informatics tools may impede the adoption of our products and may adversely impact our business.

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

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

Changes in the value of the relevant currencies may affect the cost of certain items required in our operations. Changes in currency exchange rates may also affect the relative prices at which we are able 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 currency could make our products more expensive, impacting our ability to compete. Our costs of materials from international suppliers may increase if in order to continue doing business with us they raise their prices 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.

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.

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

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

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.

We are subject to existing and potential additional governmental regulation 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 existing and potential future government regulation of our operations and markets. For example, export of our instruments may be subject to strict regulatory control in a number of jurisdictions. The failure to satisfy export control criteria or to obtain necessary clearances could delay or prevent shipment of products, which could adversely affect our revenue and profitability. Moreover, the life sciences industry, which is expected to be one of the primary markets for our technology, has historically been heavily regulated. There are, for example, laws in several jurisdictions restricting research in genetic engineering, which may narrow our markets. Given the evolving nature of this industry, legislative bodies or regulatory authorities may adopt additional regulation that adversely affects 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.

Regulations related to conflict minerals may 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 new 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 will incur additional costs to comply with the disclosure requirements, including costs related to conducting diligence procedures to determine the sources of conflict minerals that may be used or necessary to the production of our products and, if applicable, potential changes to components, processes or sources of supply as a consequence of such verification activities. We may face reputational harm if we determine that certain of our instruments contain minerals not determined to be conflict free or if we are unable to alter our processes or sources of supply to avoid such materials. Reputational harm could adversely affect our business, financial condition or results of operations.

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

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

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

Pursuant to Section 404 of the Sarbanes-Oxley Act, we were required to perform an evaluation of our internal control over financial reporting. While we performed this evaluation and concluded that our internal control over financial reporting was operating effectively as of December 31, 2013 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.

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, 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 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, consultants and certain academic collaborators to enter into confidentiality and assignment of inventions agreements, and by requiring our third-party manufacturing partners to enter into confidentiality agreements. 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, 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 have previously been, and any future challenges can be, costly and distract management's attention and resources. For example, we previously incurred significant legal expenses to litigate and settle a compliant seeking review of a patent interference decision of the U.S. Patent and Trademark Office. Additionally, as a result of these challenges, our patents or pending patent applications may be determined to be unpatentable to us, invalidated or unenforceable in whole or in part. Accordingly, adverse rulings from the relevant patent offices in these proceedings may negatively impact the scope of our intellectual property protection for our products and technology and may adversely affect our business.

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

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

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

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

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

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

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

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

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

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

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

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

Risks Related to Owning Our Common Stock

The price of our common stock has been, 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 it.

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 bookings, 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 or capital commitments;

•additions or departures of key personnel;

•competition from existing products or new products that may emerge;

•issuance of new or updated research or reports by securities analysts;

•fluctuations in the valuation of companies perceived by investors to be comparable to us;

•disputes or other developments related to proprietary rights, including patents, litigation matters and our ability to obtain intellectual property protection for our technologies;

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