

PACIFIC BIOSCIENCES OF CALIFORNIA INC

Form 10-K

March 23, 2011

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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, 2010

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)

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Delaware (State or other jurisdiction of incorporation or organization)	16-1590339 (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
Non-accelerated filer (Do not check if a smaller reporting company)
Accelerated filer
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

As of June 30, 2010, the last business day of the registrant's most recently completed second fiscal quarter, the registrant's common stock was not publicly traded. The registrant's common stock began trading on the NASDAQ Global Select Market on October 27, 2010. As of December 31, 2010, the aggregate market value of the voting stock held by non-affiliates of the registrant was approximately \$472.6 million, based on the

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closing price of the registrant's common stock on the NASDAQ Global Select Market on December 31, 2010.

Number of shares outstanding of the issuer's common stock as of February 28, 2011: 52,895,638

DOCUMENTS INCORPORATED BY REFERENCE:

Portions of the registrant's definitive Proxy Statement relating to its 2011 Annual Meeting of Stockholders to be held on June 23, 2011 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.

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Pacific Biosciences of California, Inc.

Annual Report on Form 10-K

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SPECIAL NOTE REGARDING FORWARD LOOKING STATEMENTS

Discussions under the captions *Business*, *Risk Factors*, and *Management's Discussion and Analysis of Financial Condition and Results of Operations* contain or may contain forward-looking statements that are based on 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*). Such statements may be signified by terms such as *anticipates*, *believes*, *could*, *seeks*, *estimates*, *expects*, *intends*, *may*, *plans*, *potential*, *predicts*, *projects*, *should*, *will*, *would* or similar expressions and the negative of such 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 these forward-looking statements. Also, forward-looking statements represent our management's beliefs and assumptions only as of the date of this report. Except as required by law, we assume no obligation to update these 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 genetic analysis. We have developed a technology to study the synthesis and regulation of DNA. Combining recent 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 on the DNA sequencing market where we have developed and introduced a third generation sequencing platform using our proprietary SMRT technology, the *PacBio RS*. The *PacBio RS* maintains many of the key attributes of currently available sequencing technologies while solving many of the inherent limitations of the first and second generation technologies, including short readlengths, limited flexibility, long time to result, complex sample preparation and risk of amplification bias. Our system provides long readlengths, flexibility in experimental design, fast time to result, and ease of use. The *PacBio RS* consists of an instrument platform that uses our proprietary consumables, which are currently comprised of our SMRT Cells and several chemical reagent kits used to format and sequence DNA samples. Our system is designed to be integrated into existing laboratory workflows and information systems. We have not yet generated revenue from our products and plan to commercially launch our first products during the second quarter of 2011.

We were 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.

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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 the 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 the RNA polymerase converts the DNA strand base for base into messenger RNA, or mRNA. The mRNA 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 additional 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 RNA, dozens of chemical modifications play important roles in cellular function.

Another source of complexity derives from the processing of RNA molecules after being transcribed from the genome. The majority of all genes have different forms of the 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.

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Recent advances in our understanding of biological complexity have highlighted the need for new tools 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 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 re-assembly. The first step of sample preparation is to break the target genome into multiple small fragments. Depending on the amount of sample DNA, the resulting fragments may be amplified into multiple copies 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 readlength. In the re-assembly phase, bioinformatics software is used to align overlapping reads, which allows the original genome to be assembled into contiguous sequence. The longer the readlength the easier it is to reassemble 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 readlength that is approximately 700 bases on average, but may be extended to 1,000 bases. These are relatively long readlengths compared with 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 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, usually taking days. This repetitive process also limits the average readlength 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 readlength, complex sample

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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 platform SMRT technology we have introduced a third generation DNA sequencing system, the PacBio *RS*, that addresses many of the limitations of the first and second generation technologies, by providing longer readlengths, increased flexibility, reduced time to result, high throughput, simplified sample preparation and elimination of amplification bias, and may also enable additional biological research, including kinetic detection, RNA transcription monitoring, RNA sequencing, protein translation and ligand binding. We refer to this new paradigm of study as SMRT Biology.

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 replicate 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*

The SMRT Cell

One of the fundamental challenges with observing a DNA polymerase 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. Within each ZMW, a single DNA polymerase molecule is anchored to the bottom of the glass surface of the ZMW 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 are dark. Only when they diffuse through 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.

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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 loaded with a different strand of DNA sample. Currently, our system can monitor 75,000 ZMWs simultaneously. The system can be set up to monitor the first set of 75,000 ZMWs on a SMRT Cell, then immediately shift to monitoring the second set of 75,000 ZMWs on the same SMRT Cell. As a result, the SMRT Cell enables the potential detection of approximately 150,000 single molecule sequencing reactions. 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

The PacBio *RS* is an instrument that conducts, monitors, and analyzes single molecule biochemical reactions in real time. The PacBio *RS* 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 readlength 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 readlengths. Our SMRT technology is designed to produce a distribution of readlengths with greater than 1,000 base pairs on average and instances of over 10,000 base pairs, which facilitates mapping and assembly. Longer readlengths require the sequencing of fewer overlapping segments, referred to as coverage, to efficiently assemble the underlying genomic structure. Long readlengths 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.

Faster time to result. With the PacBio *RS*, sample preparation to sequencing results can take less than one day. A typical sequencing run can require as little as 30 minutes of instrument time, with target polymerase speeds of one to three bases per second, compared to existing technologies which often 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.

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Ease of use. Our system is 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. It can be used with a variety of sample types and can output a range of DNA lengths. The PacBio *RS* 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 will allow for easy training and rapid adoption at customer sites.

Flexibility and granularity. The PacBio *RS* system offers multiple protocols, including standard, circular consensus, and strobe sequencing, enabling the user to optimize performance based on the needs for a particular project. 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* 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* 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. 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.

Our Products

We are preparing to enter the market with our first product, the PacBio *RS*, a third generation sequencing instrument that provides real-time information at the single molecule level. The initial application for the system is DNA sequencing, and the architectural design of the system will 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* instrument and proprietary consumables, including SMRT Cells and reagent kits, providing a complete solution to the customer.

The PacBio RS

The PacBio *RS* 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 robotics perform reagent mixing and prepare 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*, responsible for the secondary processing of the sequencing data being produced on the SMRT Cells. The PacBio *RS* has been designed to allow for performance improvements without an upgrade or replacement of the instrument hardware.

Consumables

To run our PacBio *RS*, 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*. 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.

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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 and restriction enzymes. 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.

Market Opportunity

The market for sequencing products is large and is expected to grow significantly. In 2009, the sequencing market was estimated to be \$1.2 billion, which is comprised of \$600 million and \$600 million for first and second generation sequencing, respectively, and is expected to grow to more than \$3.6 billion by 2014 according to a report commissioned on our behalf and conducted by Scientia Advisors, a life sciences consulting firm. The growth in this market is expected to be driven by increases in the demand for sequencing products from both research institutions and commercial companies, including academic institutions, reference labs and genomics service providers, pharmaceutical companies and agriculture biology, or AgBio, companies.

The primary areas of market growth are expected to be genomics, increasing from approximately \$700 million in 2009 to \$1.9 billion by 2014, and AgBio, increasing from approximately \$200 million in 2009 to \$1.3 billion by 2014. Historically, improvements in tools have driven growth in demand. We believe the emergence of third generation sequencing products, including our products, along with improvements in existing second generation products, will contribute to and comprise an important facet of this growth.

There are a number of emerging markets for sequencing-based tests, including molecular diagnostics, which represent significant potential opportunities for our products. For example, the market for sequence-based molecular diagnostics is estimated to be \$1.6 billion in 2014 according to Scientia Advisors.

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, high throughput 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 the DNA sequencing market. We will initially sell our products into the rapidly growing DNA sequencing market. We believe our third generation sequencing technology will address most of the limitations in current sequencing technologies and enable a wide range of experiments and applications. We believe that the introduction of the PacBio RS will expand the market for genetic analysis tools.

Continually enhance product performance to increase market share. The design of the PacBio RS will allow for significant performance improvements without an upgrade or 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.

Leverage platform to develop and launch additional applications. We plan to leverage our SMRT technology platform to develop new applications targeting kinetic detection, RNA transcription

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monitoring, RNA sequencing, protein translation and ligand binding. We believe these applications will 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 have launched the PacBio DevNet, a software developer's open network 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 open source.

Marketing and Sales

We market our products through a direct sales force in North America and Europe and recently established a presence in Asia to service the Asia Pacific market. Our sales strategy involves the use of a combination of sales managers, sales representatives and field application specialists. As of December 31, 2010, we had eleven sales managers and sales representatives and ten field application specialists. We expect to increase our sales force as we expand our business.

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 with advanced degrees, and generally have extensive experience in academic research and core sequencing lab experience.

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

We are targeting customers that include genome centers, clinical, government and academic institutions, genomics service providers and agricultural companies. In general, our customers will isolate, prepare and analyze genetic samples using the PacBio RS in their own research labs to address their specific applications and scientific questions. For example, customers in academic research institutions may have DNA samples isolated from human cancer patients while AgBio companies may have DNA samples isolated from different strains of corn or other crops.

We instituted a limited production release program pursuant to which we received orders for eleven limited production release instruments from entities such as genome centers, clinical, government and academic institutions and agricultural companies. This program was designed to help us garner quality feedback on the product prior to our full commercial launch. We received orders for our limited production release instrument from Baylor College of Medicine, the Broad Institute of MIT and Harvard, Cold Spring Harbor Laboratory, the U.S. Department of Energy Joint Genome Institute, The Genome Center at Washington University, Monsanto Company, the National Cancer Institute/SAIC-Frederick, the National Center for Genome Resources, the Ontario Institute for Cancer Research, Stanford University and Wellcome Trust Sanger Institute. During 2010, we shipped all eleven PacBio RS limited production release instruments. During the LPR testing period, which we expect to last through the first quarter of 2011, we will work with these customers to obtain feedback and plan to incorporate relevant improvements into the commercial release version of the PacBio RS.

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Backlog

As of December 31, 2010, our backlog was approximately \$24.0 million, comprised of 38 systems, including PacBio *RS* limited production release instruments shipped in 2010. 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 deliver all orders in our backlog by December 31, 2011.

Manufacturing

Our principal manufacturing facilities are located at our headquarters in Menlo Park, California. We currently manufacture our instruments in-house. Over time, we intend to outsource various sub-assemblies to third-party manufacturers, but we expect to continue to conduct the final assembly in-house. 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 suppliers and have established a supplier certification program. We purchase components through purchase orders and generally do not maintain large volumes of inventory. Some of the components required in our instruments are currently either sole sourced or single sourced.

Service and Support

Service for our instruments is performed by our field service engineers. As of December 31, 2010, we employed fourteen field service engineers, and we intend to hire additional field service engineers as we grow our business. Our field service engineers are trained in-house, building, testing and troubleshooting instruments on our factory floor before being qualified to service instruments installed at customer sites.

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 for these activities was \$111.8 million, \$75.9 million and \$38.0 million during 2010, 2009, and 2008, respectively.

We plan to continue investment in research and development to support the ongoing development of chemistry components and protocols to enhance overall system performance. Our goals are to continuously improve sequencing readlength, raw read accuracy and the number of reactions on each SMRT Cell, as well as to develop and introduce into the marketplace new applications that will take full advantage of our single molecule, real-time detection technology. In addition, our engineering teams will continue their focus on increasing instrument component and system reliability, reducing costs, increasing sample throughput, and implementing additional system flexibility and versatility.

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 give us an advantage over competitors or potential competitors.

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Our current patent portfolio, including patents exclusively licensed by 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, reagents for use in nucleic acid sequencing, including phospholinked nucleotides, and other methods for analyzing biological samples, 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, 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, 2010, we own or hold exclusive licenses to 55 issued U.S. patents, 135 pending U.S. patent applications, six granted foreign patents and 158 pending foreign patent applications, including foreign counterparts of U.S. patent and patent applications. The full term of these issued U.S. patents will expire between April 17, 2016 and May 9, 2028

Of these patents and patent applications, 19 issued U.S. patents, seven pending U.S. patent applications, one granted foreign patent and six 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. These patents and patent applications are directed to the core SMRT sequencing methods and systems and other analysis methods, and to ZMW arrays used in our current and planned products. The license agreement provides us with the exclusive right to make, use, sell, offer for sale, lease, import, export or otherwise dispose of products covered by the licensed patents in all fields of use. In exchange, we are obligated to make certain royalty payments to Cornell, including a minimum annual royalty payment, and meet certain reporting and other requirements to Cornell. We are also obligated to reimburse Cornell for the costs of prosecuting the patents and patent applications that are subject to the license. The research leading to the licensed technology was funded by the U.S. government and therefore our license from Cornell is subject to U.S. government march-in rights. Cornell may terminate its agreement with us if we are in default of our payment or reporting obligations, are in material breach of the agreement, or fail to fulfill our diligence obligations with respect to commercializing products using the licensed technology.

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. Under the terms of this license agreement, we have exclusive rights to make, have made, sell, offer to sell, have sold, use, import and have imported, products that practice the invention claimed in the patent in certain sequencing-related fields. In exchange, we are obligated to make certain royalty and milestone payments to IURTC, and to meet certain reporting requirements to IURTC. We are also obligated to reimburse IURTC for the costs of prosecuting the patents and patent applications that are subject to the license. The research leading to the licensed technology was funded by the U.S. government and therefore our license from IURTC is subject to U.S. government march-in rights. IURTC may terminate its agreement with us if we are in default of our payment or record keeping obligations, are in material breach of the agreement, or fail to fulfill our diligence obligations with respect to commercializing products using the licensed technology.

In addition, we have entered into a license agreement with Stanford University, or Stanford, for U.S. Patent No. 7,297,532, referred to as the 532 patent, which relates to immobilized ribosomes for use in analysis of ribosomal activity. Under the terms of this license agreement, we have exclusive rights to make, have made, use, import, offer to sell and sell products that would practice the invention claimed in the patent in certain fields of use until June 8, 2018, after which the license will become non-exclusive until the 532 patent expires. In

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exchange, we are obligated to make certain royalty and license maintenance payments to Stanford, and to meet certain reporting and other obligations to Stanford. We are also obligated to reimburse Stanford for all patenting expenses associated with the 532 patent, including maintenance fees and costs associated with any interference or reexamination matters. The research leading to the 532 patent was funded by the U.S. government and therefore our license from Stanford is subject to U.S. government march-in rights. Stanford may terminate its agreement with us if we are in default of our payment or reporting obligations, are in breach of any provision of the agreement, or fail to fulfill our diligence obligations with respect to commercializing products relating to the 532 patent.

We have also entered into a license agreement with GE Healthcare Bio-Sciences Corp, or GE Healthcare, under several U.S. and foreign patents and pending patent applications related to labeled nucleoside polyphosphate compounds. Under the terms of the license, we have the non-exclusive right to make, have made, import, use, distribute, offer to sell and sell products that practice the inventions claimed in the patents. In exchange, we are obligated to make certain royalty and other payments to GE Healthcare. GE Healthcare may terminate its agreement with us if, among other things, we are in breach of the agreement.

In June 2010, we entered into a collaboration agreement with Gen-Probe Incorporated, or Gen-Probe, regarding the research and development of instruments integrating our SMRT technologies and Gen-Probe's sample preparation technologies for use in clinical diagnostics. Subject to customary termination rights, the initial term of the collaboration will end on the earlier of (i) December 15, 2012 and (ii) six months after we achieve certain development milestones. During the collaboration period, each party will be free to sell instrument systems that incorporate its own technology but, subject to limited exceptions, neither party may jointly develop integrated sequencing systems for clinical diagnostics with any third party nor license its technology to any third party for such use. In addition, the collaboration agreement provides each party with preferred access to certain products of the other party when commercially available, both during and after the collaboration period.

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., Life Technologies Corporation and Roche Applied Science. Some of these companies have or will have greater financial, technical, research and other resources than us. They may 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. These emerging potential competitors include Complete Genomics, Inc. and Oxford Nanopore Technologies Ltd..

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 readlength, fast time to result and flexibility, as well as the breadth and depth of current and future applications.

Employees

As of December 31, 2010, we had 431 full-time employees. Of these employees, 217 were in research and development, 104 were in operations, 64 were in sales, marketing and service, and 46 were in general and administration. With the exception of our field-based sales and service teams, all of our employees are located at our headquarters in Menlo Park, California. None of our employees are represented by labor unions or are

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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.pacificbiosciences.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.

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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 are a development stage company with limited operating history.

We may never achieve commercial success and have not yet commercially launched our first product. We have no historical financial data upon which to base our projected revenue. We have limited historical financial data upon which to base our planned operating expense or upon which to evaluate us and our 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;

comply with evolving regulatory requirements applicable to our products;

anticipate and adapt to changes in our market;

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

maintain and develop strategic relationships with vendors and manufacturers to acquire necessary materials for the production of our products;

implement an effective marketing strategy to promote awareness 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;

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

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 have not generated revenue from product sales to date. We expect to incur increasing costs as we grow our business. 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.

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

Since we have not yet commercialized our products, we cannot be sure that they will gain acceptance in the marketplace. Our success depends, in part, on our ability to develop products that displace or supplement current technology, as well as to expand the market for genetic analysis to include new applications that are not practical with current technologies. To accomplish this, we must develop and successfully commercialize our SMRT technology for use in a variety of life science applications. There can be no assurance that we will be successful in securing customers for our products, in particular, our first product which is focused on DNA sequencing. Furthermore, we cannot guarantee that the design of our products, including the initial specifications and any enhancements or improvements to those specifications, 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 fails to develop or grows more slowly than anticipated, if competitors develop better or more cost-effective products or if we are unable to develop a significant customer base, our future sales and revenue would be materially harmed and our business may not succeed.

The products we expect to introduce are highly complex, with unknown support requirements.

In light of the highly complex technology involved in our products, there can be no assurance that we will be able to successfully complete the development or manufacture of our products or obtain sufficient reliability for commercial launch. In addition, there can be no assurance that we will be able to successfully provide adequate support for our products. If our products have reliability or other quality issues or require unexpected levels of support, our reputation and business could be harmed. We cannot estimate with any certainty the cost of service and support. We intend to ship our Pac Bio RS instruments with one year of service included in the purchase price with an option to purchase an additional year of service. If service and support costs are more than we anticipate, our business and operations may be adversely affected.

We may not be able to produce instruments with the specifications required by our customers.

We have developed performance standards for our commercial products that may not be achieved using our current design and manufacturing processes. If the actual performance of the commercial instrument deviates substantially from our target specifications or is below the performance mandated by our customers, customer demand may be negatively affected. Customers may refuse to accept our products in a timely manner or at all, which would adversely affect our revenue. Any inability to meet performance standards may materially impact the commercial viability of our products and harm our business.

We may be unable to manufacture our 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 commercialize our products, we will need to supply our customers with consumable kits to be used with our instruments. We have limited experience manufacturing these consumable kits. For example, the manufacture of our SMRT Cells involves complex manufacturing processes. Since we are in an early phase of producing SMRT Cells, our current manufacturing yields are low and therefore the cost of manufacturing these products is high. There is no assurance that we will be able to manufacture our consumable kits or SMRT Cells so that they consistently achieve the product specifications and quality that our customers expect. 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 capacity for our consumable kits or SMRT Cells to meet anticipated demand. An inability to manufacture consumable kits and SMRT Cells that consistently meet specifications, in necessary quantities and at commercially acceptable costs will have a negative material impact on our business.

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We may never earn revenue from our orders in backlog.

Our backlog represents product orders from our customers that we have confirmed and for which we have not yet recognized revenue. We may never ship products represented by this backlog or 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 not to be completed or delayed, 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 will suffer and we may have write-offs associated with excess or obsolete inventory.

Rapidly changing technology in life sciences could make the products we are developing obsolete unless we continue to develop and manufacture 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 which have unproven market demand, and new products and services developed by us may not gain market acceptance. Our inability to gain market acceptance of new products could harm our future operating results. Our future success also depends on our ability to manufacture new and improved products to meet customer demand in a timely and cost-effective manner, including our ability to resolve manufacturing issues that may arise as we commence production of these complex products. Unanticipated difficulties or delays in replacing existing products with new products or in manufacturing improved or new products in sufficient quantities to meet customer demand could diminish future demand for our products and harm our future operating results.

We may be unable to develop our future commercial applications.

Our future business depends on our ability to execute on our plans to develop, manufacture, and market additional commercial applications of our SMRT technology, including SMRT Kinetic Detection, SMRT Transcription, SMRT RNA Sequencing, SMRT Translation and SMRT Ligand Binding. These future commercial applications will require significant investments of cash and resources and we may experience unexpected delays or difficulties that could postpone our ability to commercially launch these future applications, which could have a material adverse effect on our business, prospects, operating results and financial condition.

A significant portion of our potential sales depends on customers' capital spending budgets that may be subject to significant and unexpected variation.

A substantial portion of our potential product sales represent significant capital purchases by customers. Our potential customers include academic and government institutions, medical research institutions, pharmaceutical, biotechnology and chemical companies, and their capital spending budgets can have a significant effect on the demand for our products. These budgets are based on a wide variety of factors, including the allocation of available resources to make purchases, funding from government sources, the spending priorities among various types of research equipment and policies regarding capital expenditures during recessionary periods. Any decrease in capital spending or change in spending priorities of our potential customers could significantly reduce the demand for our products. Moreover, we have no control over the timing and amount of purchases by these potential customers, and as a result, revenue from these sources may vary significantly due to factors that can be difficult to forecast. We may also have to write off excess or obsolete inventory if sales of our products are not consistent with our expectations or the market requirements for our products change due to technical innovations in the marketplace. Any delay or reduction in purchases by potential customers or our inability to forecast fluctuations in demand could harm our future operating results.

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We have limited experience in sales and marketing of our products and, as a result, may be unable to successfully commercialize our products.

We have limited experience in sales and marketing of our products. Our ability to achieve profitability depends on our ability to attract customers for our products. Although sales and marketing personnel have considerable industry experience and have engaged in marketing activities for our products, we may be unable to effectively market our products. To perform sales, marketing, distribution and customer support successfully, we will face a number of risks, including:

our ability to attract, retain and manage the sales, marketing and service personnel necessary to commercialize and gain market acceptance for our technology;

the time and cost of establishing 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 initiate and execute successful commercialization activities.

We may seek to enlist third parties to assist with sales, distribution and customer support globally or in certain regions of the world. There is no guarantee, if we do seek to enter into such arrangements, that we will be successful in attracting desirable sales and distribution partners or that we will be able to enter into such arrangements on favorable terms. If our sales and marketing efforts, or those of any 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 have limited experience in manufacturing our products. If we are unable to manufacture sufficient quantities of our products with sufficient quality by ourselves or with partners in a timely manner, our ability to sell our products may be harmed.

In order to commercialize our products in volume, we need to either build sufficient internal manufacturing capacity or contract with manufacturing partners, or both. Our technology and the manufacturing process for our products is highly complex, involving a large number of unique parts, and we may encounter difficulties in manufacturing our products. There is no assurance that we will be able to meet the volume and quality requirements necessary to be successful in the market. Manufacturing and product quality issues may arise as we increase the scale of our production. If our products do not consistently meet our customers' performance expectations, our reputation may be harmed, and we may be unable to generate sufficient revenue to become profitable. Any delay or inability in establishing or expanding our manufacturing capacity could diminish our ability to develop or sell our products, which could result in lost revenue and seriously harm our business, financial condition and results of 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, in which event our business would be materially harmed.

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 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 semiconductor chips, optics, lasers and cameras. If we were 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 those components that are currently purchased from a sole or single source supplier, we have not yet arranged for alternative suppliers.

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The operations of our third-party manufacturing partners and suppliers could be disrupted by conditions unrelated to our business or operations, including the bankruptcy of the manufacturer or supplier. If our manufacturing partners or suppliers are unable or fail to fulfill their obligations to us, we might not be able to manufacture our products and satisfy customer demand 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. In order to sustain our commercial launch, which will involve multiple shipments of our products, we will need to take steps to scale the manufacturing process, including lowering the manufacturing costs of our products as well as improvements to our manufacturing yields and cycle times, manufacturing documentation, and quality assurance and quality control procedures. If we are unable to reduce our manufacturing costs and establish and maintain reliable high volume manufacturing 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, including employee strikes, inclement weather and increased fuel costs. Any failure to deliver products to our customers in a timely and accurate 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. Furthermore, if the third-party carriers damage or destroy our instrument, it could take significant time to repair or replace the instrument. In addition, some of our consumable products need to be kept at a constant temperature. If our third-party carriers are not able to maintain those temperatures during shipment, our products may be rendered unusable by our customers. The failure to deliver our products in a timely manner may harm our relationship with our customers, increase our costs and otherwise disrupt our operations.

We may encounter difficulties in managing our growth, and these difficulties could impair our profitability.

We expect to experience rapid and substantial growth, which will place a strain on our human and capital resources. If we are unable to manage this growth effectively, our business and operating results could suffer. Our ability to manage our operations and costs, including research and development, costs of components, manufacturing, sales and marketing, requires us to continue to enhance our operational, financial and management controls, reporting systems and procedures and to attract and retain sufficient numbers of talented employees, including an expansion of our executive management team. If we are unable to scale up and implement improvements to our manufacturing process, develop reliable third-party manufacturers of sub-assemblies and control systems in an efficient or timely manner, or if we encounter deficiencies in existing systems and controls, we will not be able to make available the products required to commercialize our technology successfully. Failure to attract and retain sufficient numbers of talented employees will further strain our human resources and could impede our growth.

Hugh Martin, our Chief Executive Officer, has been diagnosed with a form of cancer, and the impact of this condition on his ability to lead the company in the future may be uncertain.

Mr. Martin has informed us that he has been diagnosed with multiple myeloma, a form of cancer. Although his condition has not had any impact on Mr. Martin's performance in his role as Chief Executive Officer or on the overall management of the company, we can provide no assurance that his condition will not affect his ability to perform the role of Chief Executive Officer in the future. If Mr. Martin becomes unable to continue to perform his role as Chief Executive Officer, we would need to select a new Chief Executive Officer which we may not be able to do easily, and may require other senior management to divert part of their attention from their primary duties, which could have a material adverse effect on our business or operations.

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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. Many of these 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 our ability 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.

Adverse conditions in the global economy and disruption of financial markets may significantly harm our revenue, profitability and results of operations.

The global economy and credit and capital markets have experienced recent volatility and disruption. Volatility and disruption of financial markets could limit our customers' ability to obtain adequate financing or credit to purchase and pay for our products in a timely manner or to maintain operations, which could result in a decrease in sales volume that could harm our results of operations. General concerns about the fundamental soundness of domestic and international economies may also cause our customers to reduce their purchases. Changes in governmental banking, monetary and fiscal policies to address liquidity and increase credit availability may not be effective. Significant government investment and allocation of resources to assist the economic recovery of sectors which do not include our customers may reduce the resources available for government grants and related funding for life sciences research and development. Continuation or further deterioration of these financial and macroeconomic conditions could significantly harm our sales, profitability and results of operations.

We may need additional financing to fund our existing operations. Securities we issue to fund our operations could dilute your ownership.

We may decide to raise additional funds through public or private debt or equity financing. Such additional funds may not be available on terms acceptable to us or at all, particularly in light of recent market conditions. If we raise funds by issuing equity securities, the percentage ownership of our stockholders will be reduced, and the new equity securities may have priority rights over current investors. We may delay, limit or eliminate some or all of our proposed operations and research and development if adequate funds are not available.

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

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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 technology. 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.

We expect that our sales cycle will be lengthy and unpredictable, which will make it difficult for us to forecast revenue and may increase the magnitude of quarterly fluctuations in our operating results.

Our PacBio RS is expected to have a lengthy sales and purchase order cycle because it is a major capital item and generally requires the approval of our customers' senior management. This may contribute to substantial fluctuations in our quarterly operating results, particularly during the periods in which our sales volume is low. Because of these fluctuations, it is likely that in some future quarters our operating results will fall below the expectations of securities analysts or investors. If that happens, the market price of our stock would likely decrease. These fluctuations also mean that investors will not be able to rely upon our operating results in any particular period as an indication of future performance.

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.

Any product using our SMRT technology will be 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 market acceptance or expansion, diversion of development resources, injury to our reputation and increased warranty, service and maintenance costs. We intend to ship our PacBio RS instruments with one year of service included in the purchase price with an option to purchase an additional year of service. We will provide a twelve-month warranty on the PacBio RS. The warranty is limited to replacing, repairing or giving credit for, at our option, any instrument for which a warranty claim is provided to us within the warranty period. We will also provide a warranty for our consumables, but claims must be made within 90 days from the date of delivery or the shelf life date or use by date, if earlier. 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, which could be costly and time-consuming to defend and result in substantial damages. Although we have product liability insurance, any future product liability insurance that we procure 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 do 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.

Adoption of our products by customers may depend on the availability of informatics tools, some of which may be developed by third parties.

Our commercial success may depend in part upon the development of 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 informatics tools may impede the adoption of our products and may adversely impact our business.

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Ethical, legal 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 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 used for 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. 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 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. Although we cannot predict the ultimate impact of any such new laws and regulations, or such more stringent enforcement, they will likely 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.

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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 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.

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 sales entail a variety of risks, including longer payment cycles and difficulties in collecting accounts receivable outside of the United States, currency exchange fluctuations, 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. The recent global financial downturn has led to a high level of volatility in foreign currency exchange rates and that level of volatility may continue, which could adversely affect our business, financial condition or results of operations.

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. See also our risk factor

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above titled Ethical, legal and social concerns surrounding the use of genetic information could reduce demand for our technology. 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. See also our risk factors above titled 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 cost and delay our commercialization efforts, thereby materially and adversely affecting our business and results of operations and 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. Failure to comply with these 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.

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 have in the past discovered, and may in the future discover, areas of our internal financial and accounting controls and procedures that need improvement. The rapid growth of our operations and our IPO created a need for additional resources within the accounting and finance functions in order to produce timely financial information and to ensure the level of segregation of duties 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.

We will be required to comply with Section 404 of the Sarbanes-Oxley Act in connection with our annual report on Form 10-K for the year ending December 31, 2011. We expect to expend significant resources in developing the necessary documentation and testing procedures required by Section 404. We cannot be certain that the actions we will be taking to improve our internal control over financial reporting will be sufficient, or that we will be able to implement our planned processes and procedures in a timely manner. 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.

The requirements of being a public company may strain our resources, divert management's attention and affect our ability to attract and retain qualified board members.

As a public company, we incur additional accounting, legal and other expenses associated with our public company reporting requirements. We will also incur costs associated with corporate governance requirements, including requirements under the Sarbanes-Oxley Act of 2002, the Dodd-Frank Act of 2010, as well as rules and regulations implemented by the SEC and The NASDAQ Stock Market. We expect these rules and regulations to increase our legal and financial compliance costs and to make some activities more time-consuming and costly. Furthermore, these rules and regulations could make it more difficult or more costly for us to obtain certain types of insurance, including director and officer liability insurance, and we may be forced to accept reduced policy

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limits and coverage or incur substantially higher costs to obtain the same or similar coverage. The impact of these requirements could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors, our board committees or as executive officers. We are currently evaluating and monitoring developments with respect to these rules and regulations, and we cannot predict or estimate the amount of additional costs we may incur or the timing of such costs.

New laws and regulations as well as changes to existing laws and regulations affecting public companies, including the provisions of the Sarbanes-Oxley Act of 2002 and rules adopted by the SEC and the NASDAQ, would likely result in increased costs to us as we respond to their requirements.

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, some of which are outside of our control, 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

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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.

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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, including patent licenses from Cornell Research Foundation, Indiana University Research and Technology Corporation, Stanford University and GE Healthcare Bio-Sciences Corp. As more fully described in our Prospectus, 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

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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 can be costly and distract management's attention and resources. Additionally, as a result of these challenges, our patents or pending patent applications may be determined to be unpatentable to us, invalid 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 are presently, and 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 may claim that we infringe their patent rights and may file lawsuits or engage in other proceedings against us to enforce their patent rights. We are presently involved in a lawsuit filed by Helicos Biosciences Corporation that alleges that our products infringe patents owned and in-licensed by Helicos (see Legal Proceedings). In defending this lawsuit, we expect to incur substantial costs, and experience diversion of attention of our management and technical personnel. An unfavorable outcome in this lawsuit could result in our having to pay

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damages, royalties or both to Helicos, and could prevent us from selling some or all of our products. 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. In fact, several companies in our industry, such as Affymetrix, Inc., Life Technologies Corporation, Illumina, Inc. and Complete Genomics, Inc., are involved in patent litigation with each other. 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 could incur substantial costs, and the attention of our management and technical personnel could be diverted. 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

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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 Relating to Owning Our Common Stock

Our share price may be 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 could be subject to wide fluctuations in response to many risk factors listed in this section, and others beyond our control, including:

actual or anticipated fluctuations in our financial condition and operating results;

announcements of technological innovations by us or our competitors;

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;

announcement or expectation of additional financing efforts;

sales of our common stock by us or our stockholders;

share price and volume fluctuations attributable to inconsistent trading volume levels of our shares;

the expiration of contractual lock-up agreements with certain stockholders; and

general economic and market conditions.

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

If securities or industry analysts publish negative reports about our business, our share price and trading volume could decline.

The trading market for our common stock will be influenced by the research and reports that securities or industry analysts publish about us or our business. If one or more of the analysts who cover us downgrade our

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shares or change their opinion of our shares, our share price would likely decline. If one or more of these analysts cease coverage of our company or fail to regularly publish reports on us, we could lose visibility in the financial markets, which could cause our share price or trading volume to decline.

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

The holders of a significant number of shares of our common stock will be entitled to rights with respect to registration of such shares under the Securities Act pursuant to an investor rights agreement between such holders and us. If such holders, by exercising their registration rights, sell a large number of shares, they could adversely affect the market price for our common stock. If we file a registration statement for the purpose of selling additional shares to raise capital and are required to include shares held by these holders pursuant to the exercise of their registration rights, our ability to raise capital may be impaired. We filed a registration statement on Form S-8 under the Securities Act to register shares for issuance under our 2004 Equity Incentive Plan, 2005 Stock Plan, 2010 Equity Incentive Plan, 2010 Employee Stock Purchase Plan and 2010 Outside Director Equity Incentive Plan. Each of our 2010 Equity Incentive Plan, 2010 Employee Stock Purchase Plan and 2010 Outside Director Equity Incentive Plan provides for automatic increases in the shares reserved for issuance under the plan which could result in additional dilution to our stockholders. Once we register these shares, they can be freely sold in the public market upon issuance and vesting, subject to a 180-day lock-up period and other restrictions provided under the terms of the applicable plan and/or the option agreements entered into with option holders.

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

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

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

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

authorize our board of directors to issue, without further action by the stockholders, up to 50,000,000 shares of undesignated preferred stock and up to approximately 933,000,000 shares of authorized but unissued shares of common stock;

require that any action to be taken by our stockholders be effected at a duly called annual or special meeting and not by written consent;

specify that special meetings of our stockholders can be called only by our board of directors, the Chairman of the Board, the Chief Executive Officer or the President;

establish an advance notice procedure for stockholder approvals to be brought before an annual meeting of our stockholders, including proposed nominations of persons for election to our board of directors;

establish that our board of directors is divided into three classes, Class I, Class II and Class III, with each class serving staggered terms;

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provide that our directors may be removed only for cause; and

provide that vacancies on our board of directors may be filled only by a majority of directors then in office, even though less than a quorum.

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

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

We have approximately 933,000,000 authorized but unissued shares of common stock. Our board of directors may issue shares of common stock from this authorized but unissued pool from time to time without stockholder approval, resulting in the dilution of our existing stockholders.

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

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

ITEM 1B. UNRESOLVED STAFF COMMENTS

None

ITEM 2. PROPERTIES

Our corporate headquarters and manufacturing facilities are located in Menlo Park, California where we lease approximately 147,300 square feet of office, lab and manufacturing space. The schedule below summarizes facilities we occupy as of December 31, 2010. We consider our manufacturing facilities sufficient to meet our current and planned operational requirements. We intend to vacate the buildings with lease expirations of May 2011 when the leases expire. We intend to add new facilities as we add employees and expand our markets, and we believe that suitable additional or substitute space will be available as needed to accommodate any such expansion of our operations.

Size (Square Feet)	Lease Expiration	Functions
30,200	May 2011	Office/Lab
31,600	May 2011	Office/Lab
33,800	December 2015	Office/Training
22,300	December 2015	Manufacturing
29,400	December 2015	Manufacturing

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During December 2010, we entered into agreements to lease additional facilities next to our existing facilities in Menlo Park, California which we plan to fully occupy in 2011. The schedule below summarizes these additional facilities.

Size (Square Feet)	Lease Expiration	Functions
14,000	December 2015	Office
21,200	December 2015	Manufacturing/Lab
54,600	December 2015	Office/Lab

ITEM 3. LEGAL PROCEEDINGS

We have been involved in a patent interference with Life Technologies Corporation, or Life, related to U.S. Patent No. 7,329,492, the 492 patent, that was acquired by Life from its acquisition of Visigen Biotechnologies, Inc., and U.S. Patent Application Serial No. 11/459,182, owned by us relating to a particular method for single molecule sequencing. An interference is a phased process whereby the U.S. Patent and Trademark Office, or USPTO, determines which of two patents, or a patent and a patent application, that claim the same or overlapping subject matter, is entitled to the earliest priority date of invention, and thus which patent or patent application is entitled to be issued covering that same or overlapping subject matter.

In January 2011, we announced that the Board of Patent Appeals and Interferences of the USPTO rendered a decision in the matter. The decision cancels all patent claims by Life Technologies Corporation involved in the interference. In the ruling, the Board entered judgment against the 492 patent, holding that all of the Life claims that were involved in the interference are unpatentable to them. In reaching its decision to cancel the Life claims, the Board agreed with our assertion that the Life Technologies patent specification does not adequately disclose the claimed invention. While the Board determined that neither party was entitled to the broadest claims presented, they denied Life's request that a subset of our claims be found unpatentable. While the Board has rendered its decision and judgment, either party may appeal the decision and judgment the U.S Court of Appeals for the Federal Circuit, or seek judicial review of the decision and judgment in the United States District Court.

On August 27, 2010, we were named as a defendant in a complaint filed by Helicos Biosciences Corporation (Helicos) in the United States District Court for the District of Delaware (Case No. 1:10-CV-00735 SLR). In the complaint, Helicos alleges that we are infringing, inducing others to infringe, and contributing to the infringement by others of two patents in-licensed by Helicos and two patents owned by Helicos, by making, using, and selling our SMRT technology for single molecule sequencing of DNA and teaching customers how to use the SMRT technology and PacBio RS sequencing platform. The four patents asserted by Helicos are U.S. Patent Nos. 7,645,596 and 7,037,687 (each titled Method of Determining the Nucleotide Sequence of Oligonucleotides and DNA Molecules), 7,169,560 (titled Short Cycle Methods for Sequencing Polynucleotides), and 7,767,400 (titled Paired-end Reads in Sequencing by Synthesis). Helicos seeks a permanent injunction enjoining us from further infringement of the asserted patents, and unspecified monetary damages, including enhanced damages under 35 U.S.C. §284, costs, attorneys fees and other relief as the court deems just and proper. On October 22, 2010, Helicos filed an amended complaint naming additional defendants in the lawsuit. On November 8, 2010, we filed our answer to Helicos complaint denying Helicos allegations that our products infringe any valid claims of the patents in suit, asserting affirmative defenses of noninfringement, invalidity and unenforceability of the claims of the patents in suit, and asserting counterclaims for declaratory judgment that our products do not infringe the claims of the patents in suit, and that those claims are invalid and unenforceable. Despite our defenses and counterclaims, we cannot guarantee any outcome of this lawsuit.

An estimate of the possible loss or possible range of loss associated with the resolution of these contingencies cannot be provided with certainty or confidence, and therefore no estimate is provided and we have not recorded a liability.

We are not currently a party to any other material legal proceedings.

ITEM 4. [REMOVED AND RESERVED]

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Our common stock has been listed on the Nasdaq Global Select Market under the symbol PACB since October 27, 2010. Prior to that time, there was no public market for our stock. The following table sets forth the high and low intra-day sales prices per share for our common stock for the indicated periods.

	High	Low
Fiscal Year 2010 Quarters Ended:		
December 31, 2010 (from October 27, 2010)	\$ 17.47	\$ 11.25

 Holders of Record

As of February 28, 2011, there were approximately 329 stockholders of record of our common stock.

Dividend Policy

We have never declared or paid any cash dividend on our common stock and have no present plans to do so. We currently intend to retain any future earnings and do not expect to pay any dividends in the foreseeable future.

Performance Graph

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

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

* \$100 invested on 10/27/10 in stock or 9/30/10 in index-including reinvestment of dividends.

Fiscal year ending December 31.

	October 27, 2010	October 29, 2010	November 30, 2010	December 31, 2010
Pacific Biosciences of California Inc	\$ 100.00	\$ 102.19	\$ 76.64	\$ 96.78
NASDAQ Composite Index	100.00	100.17	99.80	105.98
NASDAQ Biotechnology Index	100.00	100.33	98.15	104.93

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Recent Sales of Unregistered Securities

From October 1, 2010 to December 31, 2010, we issued and sold an aggregate of 32,085 shares of our common stock to our employees at a price ranging from \$0.70 to \$10.84 per share for an aggregate of \$99,000 pursuant to exercises of options granted under our 2005 Stock Plan, as amended. Also during this period, 15,384 warrants were exercised using the net settlement election resulting in the purchase of 12,792 shares of common stock. The sales and issuances of securities in the transactions described above were deemed to be exempt from registration under the Securities Act of 1933, as amended (the Securities Act), in reliance upon Rule 701 promulgated under the Securities Act, as transactions pursuant to compensatory benefit plans and contracts relating to compensation as provided under Rule 701, or Section 4(2) of the Securities Act.

Use of Proceeds

Our initial public offering of common stock was effected through a Registration Statement on Form S-1 (File No. 333-168858) that was declared effective by the Securities and Exchange Commission on October 26, 2010, which registered an aggregate of 14,375,000 shares of our common stock. On November 1, 2010, we sold 12,500,000 shares of common stock at an initial public offering price of \$16.00 per share, for aggregate gross proceeds of \$200 million. The underwriters of the offering were J.P. Morgan Securities Inc., Morgan Stanley & Co. Incorporated, Deutsche Bank Securities Inc. and Piper Jaffray & Co. On November 4, 2010, in connection with the exercise of the underwriters' over-allotment option, 1,875,000 additional shares of common stock were sold on our behalf at the initial public offering price of \$16.00 per share, for aggregate gross proceeds of \$30 million.

We paid to the underwriters underwriting discounts totaling approximately \$16.1 million in connection with the offering. In addition, we incurred expenses of approximately \$3.1 million in connection with the offering, which when added to the underwriting discounts paid by us, amount to total expenses of approximately \$19.2 million. Thus, the net offering proceeds to us, after deducting underwriting discounts and offering expenses, were approximately \$210.8 million. No offering expenses were paid directly or indirectly to any of our directors or officers (or their associates) or persons owning ten percent or more of any class of our equity securities or to any other affiliates.

As of the date of this report, there has been no material change in the use of proceeds from our initial public offering as described in our final prospectus filed with the SEC pursuant to Rule 424(b).

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This selected statement of operations data for the years ended December 31, 2010, 2009 and 2008 and selected balance sheet data as of December 31, 2010 and 2009 have been derived from our audited consolidated financial statements and related notes included elsewhere in this Form 10-K. The statement of operations data for the years ended December 31, 2007 and 2006 and the balance sheet data as of December 31, 2008, 2007 and 2006 has been derived from our audited financial statements not included in this Form 10-K.

The following selected financial data also reflects the 1-for-2 reverse stock split of our outstanding common stock effected in September 2010.

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

	2010	Years Ended December 31,			2006
		2009	2008	2007	
(in thousands, except share and per share amounts)					
Statement of Operations Data:					
Grant revenue	\$ 1,674	\$ 135	\$ 901	\$ 2,163	\$ 2,011
Operating expenses					
Research and development (1)	111,821	75,879	37,997	19,216	10,364
Sales, general and administrative (1)	30,087	12,326	7,713	6,338	3,501
Total operating expenses	\$ 141,908	\$ 88,205	\$ 45,710	\$ 25,554	\$ 13,865
Loss from operations	(140,234)	(88,070)	(44,809)	(23,391)	(11,854)
Other income (expense)					
Interest income, net	172	451	1,157	1,940	271
Other expense, net	(104)	(84)	(102)	(67)	(105)
Total other income (expense)	68	367	1,055	1,873	166
Net loss	\$ (140,166)	\$ (87,703)	\$ (43,754)	\$ (21,518)	\$ (11,688)
Basic and diluted net loss per share	\$ (14.10)	\$ (173.03)	\$ (133.82)	\$ (272.93)	*
Weighted average shares outstanding used to calculate basic and diluted net loss per share (2)	9,938,411	506,865	326,955	78,841	996
	2010	As of December 31,			2006
		2009	2008	2007	
(in thousands)					
Balance Sheet Data:					
Cash, cash equivalents and investments (3)	\$ 283,674	\$ 92,735	\$ 106,051	\$ 30,090	\$ 50,090
Working capital	272,274	85,326	102,224	27,082	48,043
Total assets	305,747	101,098	113,107	34,349	52,533
Convertible preferred stock warrant liability		226	142	151	140
Convertible preferred stock (4)		269,101	201,085	81,222	81,154
Total stockholders' equity (deficit)	279,866	(177,123)	(93,389)	(52,135)	(32,412)

- (1) Includes stock-based compensation expense. For further information, see Note 11. Stock Option Plans in the Notes to Consolidated Financial Statements of this Form 10-K.

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- (2) For further information, see Note 11. Net Loss Per Share in the Notes to Consolidated Financial Statements of this Form 10-K for an explanation of the method used to calculate basic and diluted net loss per share of common stock and the weighted-average number of shares used in computation of the per share amounts.
- (3) As of December 31, 2010, we had cash, cash equivalents and investments of \$283.7 million, an increase over 2009 reflecting the \$210.8 million net proceeds raised through our IPO in October 2010, and \$106.1 million raised from issuance of Series F convertible preferred stock.
- (4) In connection with our IPO declared effective October 26, 2010, all outstanding convertible preferred stock converted into common stock.
- (*) Due to the limited number of weighted-average unrestricted shares of our common stock outstanding during 2006 the calculated net loss per share is not meaningful.

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

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

Overview

We develop, manufacture and market an integrated platform for genetic analysis. Combining recent advances in nanofabrication, biochemistry, molecular biology, surface chemistry and optics, we created a technology platform called single molecule, real-time, or SMRT, technology. Our initial focus is to use our SMRT technology in the DNA sequencing market where we have developed and are preparing to commercialize our first product, the PacBio RS, a third generation sequencing platform. The PacBio RS consists of an instrument platform that uses our proprietary consumables, including our SMRT Cells and reagent kits, providing a complete solution to the customer.

We are a development stage company with limited operating history and have not recognized any revenue from sales or related services resulting from our planned principal operations. We operate in a single segment and our revenue to date has come from U.S. government grants. Operations to date have been primarily focused on developing our technology, undertaking engineering activities to develop our products, conducting initial marketing of our products, and pre-production activities associated with the expected commercial launch in 2011. We have financed our operations primarily through the issuance of convertible preferred stock resulting in \$364.2 million in net proceeds and the issuance of 14.4 million shares of common stock at \$16.00 per share related to our initial public offering resulting in \$210.8 million in net proceeds.

Since our inception, we have incurred significant net losses and we expect to continue to experience significant losses as we invest in research and development, sales and administrative infrastructure. As of December 31, 2010, we had a deficit accumulated during the development stage of \$332.2 million. We incurred net losses of \$140.2 million, \$87.7 million and \$43.8 million in 2010, 2009 and 2008, respectively.

Basis of Presentation

Revenue

To date, our revenue has consisted of amounts earned from government grants. The terms of these grants generally provide for reimbursement of certain research and development expenditures incurred by us over a contractually defined period. We expect to receive continued revenue in the future from government grants. In 2010, we earned approximately \$1.7 million in funding from U.S. government grants.

Deliveries and subsequent customer acceptances of limited production release units of our PacBio RS will not result in revenue recognition as the contracts pursuant to which the units were delivered require an upgrade to full commercial release specifications. Any amounts collected from customers will be deferred until such time as the full commercial release unit has been accepted at which time revenue will be recognized.

Operating Expenses

Research and Development Expense. Research and development expense consists primarily of expenses for personnel engaged in the development of our SMRT technology, the design and development of our products,

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including the PacBio RS, SMRT Cells and reagent kits and the scientific research necessary to produce commercially viable applications of our technology. These expenses also include prototype-related expenditures, development equipment and supplies, facilities costs and other related overhead. We generally expense research and development costs as they are incurred unless we make non-refundable upfront payments for delivery of future goods or services, in which case we capitalize the payments and recognize the expense in the statement of operations when the goods or services are delivered.

Since inception, we have incurred approximately \$266.2 million of research and development expense. During 2010, research and development expense of \$111.8 million was primarily comprised of payroll-related expense and prototype materials. As we transition to commercial operations in 2011, we expect prototype expenses will decline as compared to 2010 and we expect a shift in payroll-related expense to manufacturing activities.

In the fourth quarter of 2010, we began to capitalize pre-launch instrument inventory due to the certainty of its future economic benefit as indicated by technical feasibility, customer acceptance of beta products, and the time remaining to complete full commercial release units.

Sales, General and Administrative Expense. Sales, general and administrative expense consists primarily of personnel-related expense related to our executive, legal, finance, sales, marketing, human resource, information technology and operations functions, as well as fees for professional services and facility costs. Professional services consist principally of external legal, accounting and other consulting services. We expect sales, general and administrative expense to increase as we incur additional costs related to commercializing our products and operating as a publicly traded company, including increased legal fees, accounting fees and costs of compliance with securities laws and other regulations. In addition, we expect to incur additional costs as we hire personnel and enhance our infrastructure to support the anticipated growth of our business.

Other Income and Expense

Interest Income (Expense), Net. Interest income (expense), net consists primarily of interest income earned and accretion of discounts and amortization of premiums on investment balances. Our interest income will vary each reporting period depending on our average investment balances during the period and market interest rates. Interest income (expense), net also includes interest expense relating to our loan and debt agreements repaid in 2009 and our facility financing obligations resulting from lease agreements entered into in 2010. We expect interest expense to fluctuate in the future with changes in the obligations.

Other Income (Expense), Net. Other income (expense), net consists primarily of the change in the fair value of our convertible preferred stock warrants. Outstanding convertible preferred stock warrants were classified as liabilities and were remeasured at each balance sheet date with changes in fair value recognized as other income (expense), net. We continued to adjust the liability for changes in fair value until our IPO, at which time all unexercised warrants were automatically converted into warrants to purchase common stock and the warrant liability was reclassified to additional paid-in capital.

Income Taxes

Provision for (Benefit From) Income Taxes. Since inception, we have incurred net losses and have not recorded any U.S. federal or state income tax benefits for such losses as they have been offset by valuation allowances.

Critical Accounting Policies and Estimates

Our discussion and analysis of our financial condition and results of operations are based upon our consolidated financial statements, which have been prepared in accordance with accounting principles generally

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accepted in the United States, or GAAP. The preparation of financial statements in accordance with GAAP requires us to make estimates and assumptions that affect the reported amounts of assets, liabilities, revenue, expense and related disclosures. We base our estimates and assumptions on historical experience and on various other factors that we believe to be reasonable under the circumstances. We evaluate our estimates and assumptions on an ongoing basis. The results of our analyses form the basis for making assumptions about the carrying values of assets and liabilities that are not readily apparent from other sources. Our actual results may differ, potentially materially, from these estimates under different assumptions or conditions.

We believe the following critical accounting policies involve significant areas where management applies judgments and estimates in the preparation of our financial statements.

Revenue Recognition

We currently recognize revenue from government grants. We recognize revenue when persuasive evidence of an arrangement exists, delivery has occurred or services have been rendered, the price is fixed or determinable and collectability is reasonably assured.

Government grants are made pursuant to agreements that generally provide cost reimbursement for certain types of expenditures in return for research and development activities over a contractually defined period. Revenue from government grants are recognized in the period during which the related costs are incurred, provided that the conditions under which the government grants were issued have been met.

We anticipate that our future revenue will be generated primarily from sales of our PacBio *RS* instrument and consumables including SMRT Cells, reagent kits and system service agreements. Provided the criteria for revenue recognition has been met, we generally expect to recognize instrument revenue upon delivery and customer acceptance. Service revenue is expected to consist of revenue derived from warranty and service agreements, which will be recognized in the period during which the related services are rendered. The timing of revenue recognition and the amount of revenue actually recognized in each case will be dependent upon a number of considerations and will require significant judgments and estimates based on the terms of each arrangement and the deliverables and obligations set forth therein.

Convertible Preferred Stock Warrants

Prior to our IPO in October 2010, we accounted for freestanding warrants to purchase shares of our convertible preferred stock at fair value on the balance sheet because we may have been obligated to redeem these warrants at some point in the future. The warrants were subject to remeasurement at each balance sheet date with changes in fair value recognized as other income (expense), net in the consolidated statement of operations. We continued to adjust the liability for changes in fair value until our IPO, at which time all unexercised warrants automatically converted into warrants to purchase common stock and the warrant liability was reclassified to additional paid-in capital.

During 2010, 2009 and 2008, we recorded charges (gains) of \$100,000, \$84,000, and \$(9,000), respectively, through other income (expense), net to reflect the change in the fair value of the warrants.

Stock-Based Compensation

Effective January 1, 2006, we adopted the fair value method of accounting for our stock options granted to employees which requires us to measure the cost of employee services received in exchange for the stock options based on the grant date fair value of the award. We estimated the value, and resulting cost, of stock-based compensation awards using the Black-Scholes option pricing model. The resulting cost is recognized over the period during which an employee is required to provide service in exchange for the award, generally the vesting period, which is four to five years.

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We adopted the fair value method using the prospective transition method as prior to adoption we used the minimum value method for the previously required pro forma disclosures. The prospective transition method requires us to continue to apply the intrinsic value method in future periods to equity awards outstanding as of January 1, 2006. Under the prospective transition method, any compensation costs that will be recognized from January 1, 2006 will include only (i) compensation cost for all stock-based awards granted prior to, but not yet vested as of December 31, 2005, based on the intrinsic value method and (ii) compensation cost for all stock-based awards granted or modified subsequent to December 31, 2005, net of estimated forfeitures, based on the fair value method. We amortize the fair value of our stock-based compensation for the equity awards granted after January 1, 2006 on a straight-line basis, which reflects the length of service to be provided by our employees over the vesting period of the awards.

The fair values of employee option awards were estimated on the grant date for the periods below using the Black-Scholes option pricing model with the following assumptions.

	Years Ended December 31,		
	2010	2009	2008
Expected term	6.0 years	5.7 years	7.0 years
Expected volatility	46 - 55%	46 - 48%	50 - 52%
Risk-free interest rate	1.6 - 2.7%	1.8 - 3.0%	2.8 - 3.5%
Dividend yield			

If in the future we determine that another method for calculating the fair value of our stock options is more reasonable, or if another method for calculating the above input assumptions is prescribed by authoritative guidance, the fair value calculated for our employee stock options could change significantly.

The risk-free interest rate that we use is based on the U.S. Treasury yield in effect at the time of grant with maturities approximating each grant's expected term. The expected term for our employee grants is based on our historic cancellation and exercise experience and trends as well as our expectations for future periods.

Our expected volatility is derived from the historical volatilities of several unrelated public companies within industries comparable to our business, including companies providing genetic sequencing equipment, supplies and services, because we have no trading history on our common stock. When making the selections of our peer companies and considering factors relating to volatility, we also considered the historical development of the peer enterprises relative to our planned development as it pertains to the expected term of our option grants as well as the size and financial leverage of potential comparable companies. The peer companies used in determining our expected volatility were, at the time of volatility determination, significantly larger and operationally further developed than us. However, the operational and financial growth and development of the peer companies during the period in which historical volatility were considered, were determined to be sufficiently similar to our expectations for future growth to provide a reasonable basis on which to establish our expected volatility. After considering both quantitative and qualitative factors, we combined the various factors to conclude a single volatility factor.

We estimate our forfeiture rate based on an analysis of our actual forfeitures and will continue to evaluate the appropriateness of the forfeiture rate based on actual forfeiture experience, analysis of employee turnover behavior and other factors. The effects of forfeiture adjustments during the years ended December 31, 2010, 2009, and 2008 have not been significant.

We will accumulate additional employee option data over time and incorporate market data related to our common stock which may result in future refinements to our estimates of volatility, expected term and forfeiture rates, which could materially impact the future valuation of our stock-based awards and the future stock-based compensation expense that we recognize.

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We recognized stock-based compensation expense under the fair value method related to options granted to employees and non-employees as follows (in thousands):

	2010	2009	2008
Research and development	\$ 5,733	\$ 2,314	\$ 1,183
Sales, general and administrative	3,112	748	387
Total stock-based compensation expense	\$ 8,845	\$ 3,062	\$ 1,570

As of December 31, 2010, we had \$23.2 million of unrecognized stock-based compensation expense, net of estimated forfeitures, that is expected to be recognized over a weighted-average period of 3.2 years. In future periods, our stock-based compensation expense is expected to increase as a result of our existing unrecognized stock-based compensation and as we issue additional stock-based awards to attract and retain employees and non-employee directors.

Common Stock Valuation

The fair values of the common stock underlying stock options granted through September 2010 were estimated by our board of directors, which intended all options granted to be exercisable at a price per share not less than the per share fair value of our common stock underlying those options on the date of grant. Our board of directors is comprised of a majority of non-employee directors with significant experience in the technology industry.

Given the absence of a public trading market prior to our IPO in October 2010, and in accordance with the American Institute of Certified Public Accountants Practice Aid, our board of directors exercised its reasonable judgment and considered numerous objective and subjective factors to determine the best estimate of the fair value of our common stock at each meeting at which stock option grants were approved. These factors included, among other factors, contemporaneous, independent valuations of our common stock, the rights and preferences of our convertible preferred stock relative to our common stock, the lack of marketability of our common stock, developments in our business, recent issuances of our convertible preferred stock and the likelihood of achieving a discrete liquidity event, such as an IPO, given prevailing market conditions.

Non-employee Stock-based Compensation

We account for stock options issued to non-employees based on the estimated fair value of the awards using the Black-Scholes option pricing model. The measurement of stock-based compensation expense is subject to periodic adjustments as the underlying equity instruments vest, and the resulting change in value, if any, is recognized in our statement of operations during the period the related services are rendered. Stock-based compensation expense for options granted to non-employees for 2010, 2009 and 2008 was \$1.0 million, \$0.4 million and \$0.3 million, respectively.

There is inherent uncertainty in these estimates and if different assumptions had been used, the fair value of the equity instruments issued to non-employee consultants could have been significantly different.

Impairment of Long-lived Assets

We assess impairment of long-lived assets, which include property and equipment, on at least an annual basis and test long-lived assets for recoverability when events or changes in circumstances indicate that their carrying amount may not be recoverable. Circumstances which could trigger a review include, but are not limited to, significant decreases in the market price of the asset, significant adverse changes in the business climate or legal factors, accumulation of costs significantly in excess of the amount originally expected for the acquisition or construction of the asset, current period cash flow or operating losses combined with a history of losses or a

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forecast of continuing losses associated with the use of the asset, or expectations that the asset will more likely than not be sold or disposed of significantly before the end of its estimated useful life. To date we have not recorded any impairment charges.

Leases

We categorize leases at their inception as either operating or capital leases. On certain of our lease agreements, we may receive tenant improvement allowances, rent holidays and other incentives. Rent expense is recorded on a straight-line basis over the term of the lease. The difference between rent expense accrued and amounts paid under the lease agreement is recorded as lease incentives in the accompanying balance sheets. Leasehold improvements are capitalized at cost and depreciated over the lesser of their expected useful life or the life of the lease. To the extent leasehold improvement allowances are afforded to us by the landlord, we record the tenant improvements as leasehold improvement assets with a corresponding lease incentive liability. We establish assets and liabilities for the construction costs incurred under build-to-suit lease arrangements to the extent we are involved in the construction of structural improvements or take some level of financial or construction risk prior to commencement of a lease. For further information, see Note 5. Facility Financing and Debt Obligations in the Notes to Consolidated Financial Statements of this Form 10-K.

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

Income Taxes

We are subject to income taxes in the U.S. and certain states in which we operate, and we use estimates in determining our provisions for income taxes. We use the asset and liability method of accounting for income taxes, whereby deferred tax asset or liability account balances are calculated at the balance sheet date using current tax laws and rates in effect for the year in which the differences are expected to affect taxable income.

Recognition of deferred tax assets is appropriate when realization of such assets is more likely than not. We recognize a valuation allowance against our net deferred tax assets if it is more likely than not that some portion of the deferred tax assets will not be fully realizable. This assessment requires judgment as to the likelihood and amounts of future taxable income by tax jurisdiction. At December 31, 2010, we had a full valuation allowance against all of our deferred tax assets which totaled \$135.0 million, including net operating loss carryforwards and research and development tax credits of \$117.0 million and \$12.4 million, respectively.

Effective January 1, 2007, we adopted the provisions of the Financial Accounting Standard Board, or FASB, Accounting Standards Codification, or ASC, Topic 740-10, Accounting for Uncertainty in Income Taxes. The cumulative effect of adoption resulted in no adjustment of accumulated deficit as of January 1, 2007. As of December 31, 2010, 2009, and 2008, our total unrecognized tax benefits were \$6.4 million, \$3.9 million, and \$2.0 million, respectively, of which none of the tax benefits, if recognized, would affect the effective income tax rate due to the valuation allowance that currently offsets deferred tax assets. We do not anticipate the total amount of unrecognized income tax benefits to significantly increase or decrease in the next 12 months.

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

Results of Operations*Comparison of the Years Ended December 31, 2010 and 2009*

	Years ended December 31,		Increase/ (Decrease)	% Increase/ (Decrease)
	2010 (in thousands, except percentages)	2009		
Revenue	\$ 1,674	\$ 135	\$ 1,539	*
Research and development	111,821	75,879	35,942	47%
Sales, general and administrative	30,087	12,326	17,761	144%
Loss from operations	(140,234)	(88,070)	52,164	59%
Interest income (expense), net	172	451	(279)	(62)%
Other income (expense), net	(104)	(84)	20	24%
Net loss	\$ (140,166)	\$ (87,703)	\$ 52,463	60%

* Percentage not meaningful.

Revenue

Revenue is comprised solely of government grant revenue. This revenue is dependent on the grant received, the amount of the grant and subsequent work performed pursuant to the grant. The increase in revenue realized was due to an increase in the amount of awarded government grants in 2010 as compared to 2009.

Research and Development Expense

The \$35.9 million increase in research and development expense was driven primarily by a \$15.7 million increase in purchases of material for the manufacture of prototype instruments and consumable products, and a \$15.1 million increase in personnel-related expense. The increase in personnel-related expense included significant expansion of manufacturing operations as we prepared for the commercial launch of the PacBio RS. The expansion of our manufacturing facilities resulted in a \$1.6 million increase in facility expense. Research and development expense included stock-based compensation expense of \$6.6 million and \$2.3 million during the years ended December 31, 2010 and 2009, respectively.

Sales, General and Administrative Expense

The \$17.8 million increase in sales, general and administrative expense was driven primarily by a \$12.4 million increase in personnel related expense resulting from increased headcount reflecting the continued growth of our sales, marketing and customer support organizations, a \$2.0 million increase in customer application, demonstration and marketing initiatives and a \$1.7 million increase in travel-related expense for sales and support of beta instruments in the field. Sales, general and administrative expense included stock-based compensation expense of \$3.1 million and \$0.7 million during the years ended December 31, 2010 and 2009, respectively.

Table of Contents*Loss from Operations*

The \$52.2 million increase in loss from operations was driven primarily by a \$35.9 million increase in research and development expense and a \$17.8 million increase in sales, general and administrative expense, partially offset by a \$1.5 million increase in government grant revenue.

Interest Income (Expense), Net

The decrease in interest income (expense), net was primarily due to lower interest rates on money market holdings during the majority of 2010.

Other Income (Expense), Net

The change in other income (expense), net primarily reflects the remeasurement of our warrant liability.

Net Loss

The \$52.5 million increase in net loss was driven primarily by a \$52.2 million increase in loss from operations combined with interest expense resulting from the financing obligation originating during 2010, offset by interest income from our investment portfolio.

Comparison of the Years Ended December 31, 2009 and 2008

(In thousands)	Years ended December 31,		Increase/ (decrease)	% Increase/ (decrease)
	2009	2008		
	(in thousands, except percentages)			
Revenue	\$ 135	\$ 901	\$ (766)	(85)%
Research and development	75,879	37,997	37,882	100%
Sales, general and administrative	12,326	7,713	4,613	60%
Loss from operations	(88,070)	(44,809)	43,261	97%
Interest income (expense), net	451	1,157	(706)	(61)%
Other income (expense), net	(84)	(102)	(18)	(18)%
Net Loss	\$ (87,703)	\$ (43,754)	\$ 43,949	100%

Revenue

Revenue is comprised solely of government grant revenue. This revenue is dependent on the grant received, the amount of the grant and subsequent work performed pursuant to the grant. The \$0.8 million decrease in revenue realized was due to a reduction in the amount of awarded government grants in 2009 as compared to 2008.

Research and Development Expense

The \$37.9 million increase in research and development expense was driven primarily by an \$18.9 million increase in prototype-related expenditures, equipment and development supplies, and an \$11.9 million increase in personnel-related expense resulting from increased headcount. In addition, contract services and other professional services increased \$3.0 million and information technology and facility expense increased by \$2.2 million. Research and development expense included stock-based compensation expense of \$2.3 million and \$1.2 million during 2009 and 2008, respectively.

Table of Contents*Sales, General and Administrative Expense*

The \$4.6 million increase in sales, general and administrative expense was driven primarily by a \$2.8 million increase in professional services mainly due to higher legal costs and a \$1.7 million increase in personnel-related expense resulting from increased headcount for operations activities and the expansion of the marketing team to support increased public relations and market research activities. Sales, general and administrative expense included stock-based compensation expense of \$0.7 million and \$0.4 million during 2009 and 2008, respectively.

Loss from Operations

The \$43.3 million increase in loss from operations was driven primarily by a \$37.9 million increase in research and development expense resulting from increases in proto-type-related expenditures, equipment and development supplies, and personnel-related expense combined with a \$4.6 million increase in sales, general and administrative expense primarily resulting from increased professional services and personnel-related expenses.

Interest Income (Expense), Net

The decrease in interest income was primarily a result of lower average investment balances and lower interest rates in 2009 as compared to 2008.

Other Income (Expense), Net

The change in other income (expense), net reflects the remeasurement of our convertible preferred stock warrant liability.

Net Loss

The \$43.9 million increase in net loss was driven primarily by a \$43.3 million increase in loss from operations combined with reduced interest income from our investment portfolio.

Liquidity and Capital Resources

Since our inception, and as of December 31, 2010, we have financed our operations primarily through the issuance of convertible preferred stock resulting in \$364.2 million in net proceeds and the issuance of 14.4 million shares of common stock at \$16.00 per share related to our initial public offering resulting in \$210.8 million in net proceeds.

As of December 31, 2010, we had cash, cash equivalents and investments of \$283.7 million, an increase over 2009 reflecting the \$210.8 million net proceeds raised through our IPO in October 2010, and \$106.1 million raised from issuance of Series F convertible preferred stock, offset by approximately \$122.0 million of cash used during the year to fund operations.

The following table summarizes our working capital and cash, cash equivalents and investments for the periods indicated.

	2010	December 31, 2009 (in thousands)	2008
Working capital	\$ 272,274	\$ 85,326	\$ 102,224
Cash, cash equivalents and investments	\$ 283,674	\$ 92,735	\$ 106,051

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

	Years Ended December 31,		
	2010	2009	2008
	(in thousands)		
Net cash used in operating activities	\$ (121,996)	\$ (74,838)	\$ (38,303)
Net cash provided by (used in) investing activities	(138,250)	18,594	(10,393)
Net cash provided by financing activities	318,664	67,014	119,927

During the years ended December 31, 2010, 2009 and 2008 we used cash of \$5.3 million, \$5.2 million and \$5.7 million, respectively, to fund capital expenditures. We currently anticipate making capital expenditures in the future primarily for purchases of equipment to be used in research and manufacturing scale-up.

Beyond our investment in research and manufacturing equipment, we expect to invest capital in additional production arrangements, the timing and amount of which will depend on our business and financial outlook and the specifics of the opportunity. We may also consider additional strategic investments or acquisitions. This may require us to access additional capital through equity or debt offerings. If we are unable to access additional capital, our growth will be limited due to the inability to invest in additional production facilities.

We believe that existing cash, cash equivalents and investments will be sufficient to fund our projected operating requirements for at least 12 months. Until we can generate a sufficient amount of product revenue, we expect to finance future cash needs through public or private equity offerings, debt financings or corporate collaboration and licensing arrangements.

Cash Flows From Operating Activities

Our primary uses of cash from operating activities are for personnel-related expenditures and equipment related to research and development activities. Cash used in operating activities was \$122.0 million, \$74.8 million and \$38.3 million for the years ended December 31, 2010, 2009 and 2008, respectively.

Cash used in operating activities of \$122.0 million in 2010 reflected a net loss of \$140.2 million, partially offset by aggregate non-cash charges of \$15.3 million and a net change of \$2.9 million in our net operating assets and liabilities. Non-cash charges primarily included \$9.7 million in stock-based compensation and \$5.2 million of depreciation. Net operating assets and liabilities included an increase of \$7.9 million in accounts payable, accrued expenses and other current liabilities primarily driven by payroll-related expense, and an increase of \$3.2 million in deferred revenue related to shipments of PacBio RS limited production release instruments, partially offset by an inventory increase of \$6.9 million.

Cash used in operating activities of \$74.8 million in 2009 reflected a net loss of \$87.7 million, partially offset by aggregate non-cash charges of \$7.9 million and a net change of \$4.9 million in our net operating assets and liabilities. Non-cash charges primarily included \$4.1 million of depreciation and \$3.6 million of stock-based compensation. The net change in our operating assets and liabilities was primarily a result of an increase in accounts payable of \$3.9 million and the increase in accrued and other liabilities of \$1.2 million.

Cash used in operating activities of \$38.3 million in 2008 reflected a net loss of \$43.8 million, partially offset by aggregate non-cash charges of \$5.1 million and a net change of \$0.3 million in our net operating assets and liabilities. Non-cash charges primarily included \$3.0 million of depreciation and \$2.1 million of stock-based compensation. The net change in our operating assets and liabilities was primarily a result of the increase in lease incentives and other long-term liabilities of \$0.5 million.

Table of Contents***Cash Flows From Investing Activities***

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

In 2010, the majority of our investing activities were driven by the purchase and maturities of investments achieved as a result of receiving \$210.8 million in IPO proceeds. We used approximately \$181.0 million in cash to purchase short-term investments and \$5.3 million of capital expenditures, offset by approximately \$48.0 million in maturities.

In 2009, cash provided by investing activities was \$18.6 million as a result of \$23.8 million in net investment maturities, partially offset by \$5.2 million of capital expenditures.

In 2008, cash used in investing activities was \$10.4 million as a result of \$5.7 million of capital expenditures and \$4.7 million in net investment purchases.

Cash Flows From Financing Activities

In 2010, cash provided by financing activities was \$318.7 million, comprised of \$210.8 million in IPO net proceeds received in November 2010 and \$106.1 million raised from issuance of Series F convertible preferred stock.

In 2009, cash provided by financing activities was \$67.0 million, primarily as a result of the net receipt of \$68.0 million from our sale of Series E convertible preferred stock, partially offset by principal repayments on our debt of \$1.3 million.

In 2008, cash provided by financing activities was \$119.9 million, primarily as a result of the receipt of \$119.8 million from our sale of Series E convertible preferred stock.

Contractual Obligations, Commitments and Contingencies

The following table provides summary information concerning our future contractual obligations as of December 31, 2010.

	Total	Payments due by period			More than 5 years
		Less than 1 year	1-3 years (in thousands)	3-5 years	
Operating lease obligations (1)	\$ 15,483	2,637	6,243	6,603	
Facility financing obligation	2,170	397	848	925	
Total contractual obligations	\$ 17,653	3,034	7,091	7,528	

(1) Maintenance, insurance, taxes and contingent rent obligations are excluded. See Note 6. Commitments and Contingencies in Part II, Item 8 of this Form 10-K for additional information.

Facility Financing Obligation

In December 2009 we entered into a build-to-suit lease agreement for a manufacturing and office facility where we are considered the owner of the project under GAAP. When we are considered the owner of a project, we record the shell of the facility at its fair value at the date construction commences with a corresponding facility financing obligation. Accordingly, we recorded \$3.0 million of building and leasehold improvement assets and a corresponding liability to facility financing obligation. See Note 5. Facility Financing and Debt Obligation in Part II, Item 8 of this Form 10-K for a discussion of this commitment.

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License Agreements

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

An estimate of significant payments related to licensing and other arrangements not included in the contractual obligations table include payments related to four cancelable license agreements with third parties for certain patent rights and technology. Under the terms of these agreements, we may be obligated to pay royalties based on revenue from the sales of licensed products, or minimum royalties, whichever is greater, and license maintenance fees. Pursuant to the terms of the agreements, future license maintenance fees and minimum royalty payments amount to \$0.4 million for 2011, 2012, 2013 and each year thereafter.

In addition, upon commercialization of products that incorporate the licensed technologies, we may be obligated to pay certain milestone fees of up to \$80,000. In addition, upon commercialization of products incorporating a technology provided under one license agreement, the minimum royalties owed by us under that license decrease by \$5,000 in the first year following commercialization, return to the pre-commercialization amounts for the second year following commercialization, increase by \$10,000 the third year and by \$25,000 the fourth year following commercialization of products incorporating that licensed technology.

Off-Balance Sheet Arrangements

We do not have any off-balance sheet arrangements.

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

Recent Accounting Pronouncements

During the fourth quarter of 2010, we adopted the new disclosure guidance related to the credit quality of financing receivables and the allowance for credit losses. This guidance requires companies to provide more information about the credit quality of their financing receivables in the disclosures to financial statements including, but not limited to, significant purchases and sales of financing receivables, aging information and credit quality indicators. The adoption of this accounting guidance did not have a significant impact on our consolidated financial statements.

In October 2009, the FASB issued an accounting standards update that provides application guidance on whether multiple deliverables exist, how the deliverables should be separated and how the consideration should be allocated to one or more units of accounting. This update establishes a selling price hierarchy for determining the selling price of a deliverable. The selling price used for each deliverable will be based on vendor-specific objective evidence, if available, third-party evidence if vendor-specific objective evidence is not available, or estimated selling price if neither vendor-specific nor third-party evidence is available. We will be required to apply this guidance prospectively for revenue arrangements entered into or materially modified after January 1, 2011. Our revenue to date has been limited to government grant revenue and no revenue has been recognized from the sale of our products. Therefore, adoption of this guidance is not expected to have a material impact on our financial statements.

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ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

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

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**ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTAL DATA
PACIFIC BIOSCIENCES OF CALIFORNIA, INC.**

(A development stage enterprise)

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Report of Independent Registered Public Accounting Firm

To the Board of Directors and Stockholders of

Pacific Biosciences of California, Inc.:

(A development stage enterprise)

In our opinion, the accompanying consolidated balance sheets and the related consolidated statements of operations, and consolidated statements of stockholders' equity (deficit), and of the consolidated statements of cash flows present fairly, in all material respects, the financial position of Pacific Biosciences of California, Inc. and their subsidiaries at December 31, 2010 and December 31, 2009, and the results of their operations and its cash flows for each of the three years in the period ended December 31, 2010 and cumulatively for the period from July 14, 2000 (date of inception) to December 31, 2010 in conformity with accounting principles generally accepted in the United States of America. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits. We conducted our audits of these statements in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

/s/ PricewaterhouseCoopers LLP

San Jose, California

March 23, 2011

Table of Contents**PACIFIC BIOSCIENCES OF CALIFORNIA, INC.****(A development stage enterprise)****Consolidated Balance Sheets**

(in thousands except share and per share amounts)	December 31,	
	2010	2009
Assets		
Current assets		
Cash and cash equivalents	\$ 147,650	\$ 89,232
Investments	136,024	3,503
Accounts receivable	341	
Inventory	6,864	
Prepaid expenses and other current assets	2,235	1,010
Total current assets	293,114	93,745
Property and equipment, net	12,311	7,142
Long-term assets	322	211
Total assets	\$ 305,747	\$ 101,098
Liabilities, Convertible Preferred Stock and Stockholders Equity (Deficit)		
Current liabilities		
Accounts payable	\$ 9,515	\$ 5,778
Accrued expenses and other current liabilities	7,994	2,641
Deferred revenue	3,221	
Current portion of facility financing obligation	110	
Total current liabilities	20,840	8,419
Lease incentives and other long-term liabilities	2,114	475
Facility financing obligation, less current portion	2,927	
Convertible Preferred Stock warrant liability		226
Total liabilities	25,881	9,120
Commitments and contingencies (Note 6)		
Convertible Preferred Stock, \$0.001 and \$0.0001 par value at December 31, 2010 and 2009, respectively: Authorized 50,000,000 and 116,056,382 shares at December 31, 2010 and 2009, respectively; Issued and outstanding no shares at December 31, 2010 and 60,101,338 shares at December 31, 2009		269,101
Stockholders' equity (deficit)		
Common Stock, \$0.001 par value: Authorized 1,000,000,000 shares; Issued and outstanding 52,855,267 shares at December 31, 2010 and 656,084 shares at December 31, 2009		53
Additional paid-in capital	612,001	14,877
Accumulated other comprehensive income (loss)	(21)	1
Deficit accumulated during the development stage	(332,167)	(192,001)
Total stockholders' equity (deficit)	279,866	(177,123)
Total liabilities, Convertible Preferred Stock and stockholders' equity (deficit)	\$ 305,747	\$ 101,098

See accompanying notes to the consolidated financial statements.

Table of Contents**PACIFIC BIOSCIENCES OF CALIFORNIA, INC.****(A development stage enterprise)****Consolidated Statements of Operations**

	Years Ended December 31,			Cumulative
	2010	2009	2008	Period From
(in thousands, except share and per share amounts)				July 14, 2000
				(Date of
				Inception) to
				December 31,
				2010
Grant revenue	\$ 1,674	\$ 135	\$ 901	\$ 8,598
Operating expenses				
Research and development	111,821	75,879	37,997	266,151
Sales, general and administrative	30,087	12,326	7,713	65,435
Total operating expenses	141,908	88,205	45,710	331,586
Loss from operations	(140,234)	(88,070)	(44,809)	(322,988)
Interest income, net	172	451	1,157	4,106
Other expense, net	(104)	(84)	(102)	(471)
Net loss	\$ (140,166)	\$ (87,703)	\$ (43,754)	\$ (319,353)
Basic and diluted net loss per share of Common Stock	\$ (14.10)	\$ (173.03)	\$ (133.82)	
Shares used to calculate basic and diluted net loss per share	9,938,411	506,865	326,955	

See accompanying notes to the consolidated financial statements.

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PACIFIC BIOSCIENCES OF CALIFORNIA, INC.

(A development stage enterprise)

Consolidated Statements of Stockholders' Equity (Deficit)

Period from July 14, 2000 (date of inception) to December 31, 2010

(in thousands, except share and per share amounts)	Common stock Shares	Amount	Additional paid-in capital	Deferred stock-based compensation	Accumulated other comprehensive income (loss)	Deficit accumulated during the development stage	Total stockholders equity (deficit)
Balance at inception (July 14, 2000)		\$	\$	\$	\$	\$	\$
Issuance of restricted Common Stock to founders	4,341,006		5				5
Net loss						(1)	(1)
Balance at December 31, 2000	4,341,006		5			(1)	4
Net loss						(11)	(11)
Balance at December 31, 2001	4,341,006		5			(12)	(7)
Issuance of Common Stock in connection with a license agreement	117,283						
Net loss						(15)	(15)
Balance at December 31, 2002	4,458,289		5			(27)	(22)
Net loss						(20)	(20)
Balance at December 31, 2003	4,458,289		5			(47)	(42)
Issuance of Series B Convertible Preferred Stock warrants in connection with loan and securities agreement			21				21
Issuance of Common Stock upon exercise of stock options for cash (\$0.10 to \$0.13 per share)	1,690,750		1				1
Issuance of Common Stock in connection with consulting agreements	246,752						
Issuance of Common Stock in connection with a license agreement	163,967		16				16
Non-employee stock-based compensation			3				3
Net loss						(3,611)	(3,611)
Balance at December 31, 2004	6,559,758		46			(3,658)	(3,612)
Issuance of Common Stock upon exercise of stock options for cash (\$0.10 to \$0.13 per share)	1,013,395		25				25
Conversion of Common Stock to Junior Preferred Stock at \$1.70 per share (August 2005)	(7,573,153)		(71)			(12,803)	(12,874)
Issuance of Series B Convertible Preferred Stock warrants in connection with drawdown under 2004 loan and security agreement			11				11
Deferred stock-based compensation			5,607	(5,607)			
Employee stock-based compensation under the intrinsic value method			3,199	1,070			4,269
Non-employee stock-based compensation			39				39
Net loss						(10,877)	(10,877)
Balance at December 31, 2005			8,856	(4,537)		(27,338)	(23,019)

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PACIFIC BIOSCIENCES OF CALIFORNIA, INC.

(A development stage enterprise)

Consolidated Statements of Stockholders Equity (Deficit) (Continued)

Period from July 14, 2000 (date of inception) to December 31, 2010

(in thousands, except share and per share amounts)	Common stock		Additional paid-in capital	Deferred stock-based compensation	Accumulated other comprehensive income (loss)	Deficit accumulated during the development stage	Total stockholders equity (deficit)
	Shares	Amount					
Balance at December 31, 2005	\$	\$	\$ 8,856	\$ (4,537)	\$	\$ (27,338)	\$ (23,019)
Reclassification of Preferred Stock warrants to liability			(31)				(31)
Issuance of Common Stock upon exercise of stock options for cash (\$0.70 per share)	136,695		24				24
Repurchase of unvested Junior Preferred Stock			(1)	383			382
Repurchase of unvested Common Stock	(469)		(1)				(1)
Employee stock-based compensation expense recorded under the intrinsic value method			(880)	2,716			1,836
Employee stock-based compensation expense recorded under the fair value method			48				48
Non-employee stock-based compensation			37				37
Net loss						(11,688)	(11,688)
Balance at December 31, 2006	136,226		8,052	(1,438)		(39,026)	(32,412)
Issuance of Common Stock upon exercise of stock options for cash (\$0.70 to \$1.96 per share)	137,133		88				88
Repurchase of unvested Common Stock	(6,563)						
Vesting of Common Stock options early exercised			43				43
Employee stock-based compensation expense recorded under the intrinsic value method			95	983			1,078
Employee stock-based compensation expense recorded under the fair value method			426				426
Non-employee stock-based compensation			156				156
Other comprehensive income					4		4
Net loss						(21,518)	(21,518)
Total comprehensive loss							(21,514)
Balance at December 31, 2007	\$ 266,796	\$	\$ 8,860	\$ (455)	\$ 4	\$ (60,544)	\$ (52,135)

See accompanying notes to the consolidated financial statements.

Table of Contents**PACIFIC BIOSCIENCES OF CALIFORNIA, INC.**

(A development stage enterprise)

Consolidated Statements of Stockholders Equity (Deficit)

Period from July 14, 2000 (date of inception) to December 31, 2010

(in thousands, except share and per share amounts)	Common stock		Additional paid-in capital	Deferred stock-based compensation	Accumulated other comprehensive income (loss)	Deficit accumulated during the development stage	Total stockholders equity (deficit)
	Shares	Amount					
Balance at December 31, 2007	266,796	\$	\$ 8,860	\$ (455)	\$ 4	\$ (60,544)	\$ (52,135)
Issuance of Common Stock upon exercise of stock options for cash (\$0.70 to \$6.96 per share)	310,225		267				267
Vesting of Common Stock options early exercised			65				65
Employee stock-based compensation expense recorded under the intrinsic value method			144	413			557
Employee stock-based compensation expense recorded under the fair value method			1,260				1,260
Non-employee stock-based compensation			311				311
Other comprehensive income					40		40
Net loss						(43,754)	(43,754)
Total comprehensive loss							(43,714)
Balance at December 31, 2008	577,021		10,907	(42)	44	(104,298)	(93,389)
Issuance of Common Stock upon exercise of stock options for cash (\$0.70 to \$6.96 per share)	84,241		303				303
Repurchase of unvested Common Stock	(5,178)						
Vesting of Common Stock options early exercised			79				79
Employee stock-based compensation expense recorded under the intrinsic value method			526	42			568
Employee stock-based compensation expense recorded under the fair value method			2,643				2,643
Non-employee stock-based compensation			419				419
Other comprehensive loss					(43)		(43)
Net loss						(87,703)	(87,703)
Total comprehensive loss							(87,746)
Balance at December 31, 2009	656,084	\$	\$ 14,877	\$	\$ 1	\$ (192,001)	\$ (177,123)

See accompanying notes to the consolidated financial statements.

Table of Contents**PACIFIC BIOSCIENCES OF CALIFORNIA, INC.**

(A development stage enterprise)

Consolidated Statements of Stockholders Equity (Deficit)

Period from July 14, 2000 (date of inception) to December 31, 2010

(in thousands, except per share and per share amounts)	Common stock		Additional	Deferred	Accumulated	Deficit	Total
	Shares	Amount	Paid-in	Stock-Based	Other	Accumulated	Stockholders
			Capital	Compensation	Income	During the	Equity
					(Loss)	Development	(Deficit)
						Stage	
Balances at December 31, 2009	656,084	\$	\$ 14,877	\$	\$ 1	\$ (192,001)	\$ (177,123)
Conversion of redeemable convertible preferred stock to common stock at initial public offering	37,183,523	37	374,927				374,964
Conversion of warrants from warrants for preferred stock to warrants for common stock			326				326
Elimination of fractional shares resulting from reverse stock split	(25)		(1)				(1)
Issuance of common stock from Initial public offering, net of issuance costs	14,375,000	15	210,766				210,781
Issuance of Common Stock upon exercise of stock options for cash	606,963	1	707				708
Issuance of Common Stock to consultant	20,930		281				281
Issuance of Common Stock in connection with exercise of warrants	12,792						
Vesting of Common Stock options early exercised			428				428
Employee stock-based compensation expense recorded under the intrinsic value method			845				845
Employee stock-based compensation expense recorded under the fair value method			7,880				7,880
Nonemployee stock-based compensation			965				965
Other comprehensive loss					(22)		(22)
Net loss						(140,166)	(140,166)
Total comprehensive loss							(140,188)
Balances at December 31, 2010	52,855,267	\$ 53	\$ 612,001	\$	\$ (21)	\$ (332,167)	\$ 279,866

See accompanying notes to the consolidated financial statements.

Table of Contents**PACIFIC BIOSCIENCES OF CALIFORNIA, INC.****(A development stage enterprise)****Consolidated Statements of Cash Flows**

(in thousands)	Years Ended December 31,			Cumulative
	2010	2009	2008	Period From July 14, 2000 (Date of Inception) to December 31, 2010
Cash flows from operating activities				
Net loss	\$ (140,166)	\$ (87,703)	\$ (43,754)	\$ (319,353)
Adjustments to reconcile net loss to net cash used in operating activities				
Depreciation	5,160	4,104	2,987	15,616
Stock-based compensation	9,690	3,630	2,127	23,338
Amortization of deferred financing costs			13	59
Change in Convertible Preferred Stock warrant liability fair value	100	84	(9)	283
Other items	359	110	10	381
Changes in assets and liabilities				
Accounts receivable	(341)			(341)
Inventory	(6,864)			(6,864)
Deferred revenue	3,221			3,221
Prepaid expenses and other current assets	(1,225)	27	(78)	(1,824)
Other long-term assets	(111)	(57)	(26)	(355)
Accounts payable	3,637	3,891	(223)	9,373
Accrued expenses and other current liabilities	4,245	1,168	156	6,365
Lease incentives and other long-term liabilities	299	(92)	494	775
Net cash used in operating activities	(121,996)	(74,838)	(38,303)	(269,326)
Cash flows from investing activities				
Purchase of property and equipment	(5,259)	(5,177)	(5,703)	(22,720)
Purchase of investments	(180,964)	(25,429)	(36,376)	(304,294)
Sales and maturities of investments	47,973	49,200	31,686	167,395
Net cash provided by (used in) investing activities	(138,250)	18,594	(10,393)	(159,619)
Cash flows from financing activities				
Proceeds from issuance of Convertible Preferred Stock, net	106,145	68,010	119,831	364,199
Proceeds from exercise of Common Stock options	1,738	311	489	3,435
Proceeds from exercise of Junior Preferred Stock options		1	7	20
Proceeds from issuance of Common stock in IPO, net of issuance costs	210,781			210,781
Repurchases of Common Stock		(8)		(13)
Repurchases of Junior Preferred Stock				(1,727)
Proceeds from issuance of notes payable				4,037
Payment of notes payable		(1,300)	(400)	(4,137)
Net cash provided by financing activities	318,664	67,014	119,927	576,595
Net increase in cash and cash equivalents	58,418	10,770	71,231	147,650
Cash and cash equivalents at beginning of period	89,232	78,462	7,231	
Cash and cash equivalents at end of period	\$ 147,650	\$ 89,232	\$ 78,462	\$ 147,650

Supplemental disclosure of cash flow information

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Interest paid	\$		\$ (30)		\$ (92)		\$ (584)
Supplemental disclosure of non-cash investing and financing activities							
Issuance of Convertible Preferred Stock warrants							70
Assets acquired under facility lease		2,971					2,971
Additions to property and equipment under tenant improvement allowances		1,910					1,910
Conversion of convertible preferred stock to common stock upon IPO		374,965					374,965
Reclassification of Convertible Preferred Stock warrants to liabilities							31
Reclassification of preferred warrants to common stock warrants		326					326
Issuance of common stock related to convertible preferred stock offering		281					281
Vesting of stock options related to early exercises		428					428

See accompanying notes to the consolidated financial statements.

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PACIFIC BIOSCIENCES OF CALIFORNIA, INC.

(A development stage enterprise)

Notes to Consolidated Financial Statements

1. Overview

Pacific Biosciences of California, Inc., (Pacific Biosciences , PacBio , we , us) is developing and commercializing a platform for single molecule real-time detection of biological events. Our initial focus is on the DNA sequencing market where we have developed and introduced a third generation sequencing platform. Since inception, substantially all of our resources have been invested in the development and initial commercialization of our single molecule, real-time technologies.

We continue to report as a development stage enterprise since planned principal operations have not yet commenced. Revenue recognized since inception has been limited to research grants received from government grants and does not constitute the commencement of our principal operations.

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

Reverse Stock Split

On September 30, 2010, we effected a 1-for-2 reverse stock split of our outstanding common stock and a proportional adjustment to the conversion ratios for each series of preferred stock. Accordingly, all share and per share amounts for all periods presented in these consolidated financial statements and notes thereto, have been adjusted retroactively, where applicable, to reflect this reverse stock split and adjustment of the preferred stock conversion ratio.

Initial Public Offering

On October 26, 2010, our registration statement on Form S-1 relating to our initial public offering (IPO) was declared effective by the Securities and Exchange Commission (SEC) and our IPO closed on November 1, 2010, whereby we sold 12,500,000 shares of common stock at a price of \$16.00 per share. The shares began trading on the NASDAQ Global Select Market under the trading symbol PACB on October 27, 2010. Subsequently on November 1, 2010, our underwriters exercised their overallotment option to purchase an additional 1,875,000 shares of common stock at \$16.00 per share, which transaction closed on November 4, 2010. We received net proceeds of approximately \$210.8 million from the initial public offering, including proceeds from the underwriter overallotment option, net of underwriting discounts, commissions, and offering costs.

In connection with the IPO, all outstanding convertible preferred stock converted into common stock, warrants to purchase convertible preferred stock converted into warrants to purchase common stock, and the convertible preferred stock warrant liability was reclassified to stockholders equity.

2. Summary of Significant Accounting Policies

Basis of Presentation and Consolidation

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

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PACIFIC BIOSCIENCES OF CALIFORNIA, INC.

(A development stage enterprise)

Notes to Consolidated Financial Statements (Continued)

2. Summary of Significant Accounting Policies (Continued)

Use of Estimates

The preparation of financial statements in conformity with GAAP requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenue and expense during the reporting periods. Our estimates include, but are not limited to, useful lives assigned to long-lived assets, the valuation of common and preferred stock and related warrants and options, stock-based compensation expense, provisions for income taxes, inventory and contingencies. Actual results could differ from our estimates, and such differences could be material to our financial position and results of operations.

Fair Value of Financial Instruments

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

As a basis for determining the fair value of certain of our financial instruments, we utilize a three-tier value hierarchy which prioritizes the inputs used in measuring fair value as follows: (Level I) observable inputs such as quoted prices in active markets; (Level II) inputs other than the quoted prices in active markets that are observable either directly or indirectly; and (Level III) unobservable inputs in which there is little or no market data which requires us to develop our own assumptions. This hierarchy requires us to use observable market data, when available, and to minimize the use of unobservable inputs when determining fair value. Our financial assets and liabilities that are measured at fair value on a recurring basis consist of cash equivalents, investments and warrant liabilities.

All of our cash equivalents, which include money market funds, are classified within Level I of the fair value hierarchy because they are valued using quoted market prices. Our investments are classified as Level II instruments based on other observable inputs. Our warrant liability is classified within Level III of the fair value hierarchy.

Table of Contents**PACIFIC BIOSCIENCES OF CALIFORNIA, INC.**

(A development stage enterprise)

Notes to Consolidated Financial Statements (Continued)**2. Summary of Significant Accounting Policies (Continued)**

Assets and liabilities measured at fair value are classified in their entirety based on the lowest level of input that is significant to the fair value measurement. Our assessment of the significance of a particular input to the entire fair value measurement requires management to make judgments and consider factors specific to the asset or liability. The following table sets forth our financial assets and liability that were measured at fair value as of December 31, 2010 and 2009 by level within the fair value hierarchy (in thousands).

	December 31, 2010				December 31, 2009			
	Level I	Level II	Level III	Total	Level I	Level II	Level III	Total
Assets								
Money Market Funds	\$ 118,462	\$	\$	\$ 118,462	\$ 87,464	\$	\$	\$ 87,464
Commercial Paper		59,573		59,573				
Corporate Debt Securities		49,970		49,970		3,503		3,503
U.S. Government and Agency Securities		47,141		47,141				
Total assets measured at fair value	\$ 118,462	\$ 156,684	\$	\$ 275,146	\$ 87,464	\$ 3,503	\$	\$ 90,967
Liabilities								
Convertible Preferred Stock warrants	\$	\$	\$	\$	\$	\$	\$ 226	\$ 226
Total liabilities measured at fair value	\$	\$	\$	\$	\$	\$	\$ 226	\$ 226

We adjusted the warrant liability for changes in fair value until our IPO, at which time all unexercised warrants were automatically converted into warrants to purchase common stock and the warrant liability was reclassified to additional paid-in capital. The change in the fair value of the Level III convertible preferred stock warrant liability is summarized below (in thousands):

	Years Ended December 31,		
	2010	2009	2008
Fair value at beginning of period	\$ 226	\$ 142	\$ 151
Change in fair value recorded in other expense, net	100	84	(9)
Liability reclassified to additional paid-in capital	(326)		
Fair value at end of period	\$	\$ 226	\$ 142

Cash and cash equivalents

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

Investments

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We invest our cash balances exceeding short-term operating needs in short-term investment grade commercial paper, government bonds and corporate obligation notes. We classify all of our investments as

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PACIFIC BIOSCIENCES OF CALIFORNIA, INC.

(A development stage enterprise)

Notes to Consolidated Financial Statements (Continued)

2. Summary of Significant Accounting Policies (Continued)

available-for-sale and record the estimated fair value of these investments on the balance sheets, with unrealized gains and losses, if any, reported as a component of accumulated other comprehensive income (loss) in stockholders' equity (deficit). Debt securities are adjusted for amortization of premiums and accretion of discounts, and such amortization and accretion are reported as a component of interest income. Realized gains and losses are recorded as a component of other expense, net. Realized gains and losses have not been material for all periods presented.

We periodically review our investments for potential impairment and consider investments impaired when a decline in fair value is deemed by us to be other-than-temporary. If cost exceeds fair value, we consider, among other factors, the duration and extent to which cost exceeds fair value, the financial strength of the issuer, and our intent and ability to hold the investment to maturity. Once a decline in value is deemed to be other-than-temporary, an impairment charge is recorded and a new cost basis in the investment is established. No impairment losses were recognized from inception through December 31, 2010.

Concentration of Credit Risk

Financial instruments that potentially subject us to a concentration of credit risk consist of cash, cash equivalents investments and accounts receivable. Cash balances are deposited with two domestic financial institutions and deposits may, from time to time, exceed federally insured limits. Cash equivalents consist primarily of investments in money market funds. We have not experienced any losses on our deposits of cash, cash equivalents, investments or accounts receivable.

Certain Risks and Uncertainties

We are subject to risks common to companies in the development stage, including but not limited to, development of new products, development of markets and distribution channels, dependence on key personnel, competing with established brands and the ability to obtain additional capital as needed to fund our product development plans. To date, we have been funded by public and private equity and debt financings. Our success is dependent upon our ability to raise additional capital and to successfully develop and market our products. Any significant delays in the development or marketing of products could have a material adverse effect on our business and financial results.

We have chosen to source certain critical components from single source suppliers. If we were required to purchase these components from an alternative source, it could take several months or longer to qualify the alternative sources.

Inventory

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

Property and Equipment, Net

Property and equipment are generally stated at cost, net of accumulated depreciation. Depreciation is computed using the straight-line method over the estimated useful life of the asset, generally two to three years

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PACIFIC BIOSCIENCES OF CALIFORNIA, INC.

(A development stage enterprise)

Notes to Consolidated Financial Statements (Continued)

2. Summary of Significant Accounting Policies (Continued)

for computer equipment and software, three to seven years for furniture and fixtures, three years for lab equipment and 30 years for buildings. Leasehold improvements are depreciated over the shorter of the lease term or the estimated useful life of the related asset. Major improvements are capitalized, while maintenance and repairs are expensed as incurred.

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

Impairment of Long-Lived Assets

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

Revenue Recognition

Government grants are agreements that generally provide cost reimbursement for certain types of expenditures in return for research and development activities over a contractually defined period. Revenue from government grants is recognized in the period during which the related costs are incurred, provided that the conditions under which the government grants were provided have been met.

Deferred revenue primarily represents amounts paid by customers in advance related to our limited production release PacBio RS units which are expected to be upgraded to full commercial specifications in the future.

Research and Development

Research and development expense consists of costs incurred in the development of our SMRT technology and our products, including our PacBio RS instrument, SMRT Cells and reagent kits, as well as costs incurred under government grants. We expense research and development costs to operations as incurred. However, we defer and capitalize non-refundable advance payments made for research and development activities until the related goods are received or the related services are rendered.

Leases

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

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PACIFIC BIOSCIENCES OF CALIFORNIA, INC.

(A development stage enterprise)

Notes to Consolidated Financial Statements (Continued)

2. Summary of Significant Accounting Policies (Continued)

lease. Tenant improvements afforded to us by landlord incentives are recorded as leasehold improvement assets with corresponding lease incentives liabilities.

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

Income Taxes

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

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

Stock-based Compensation

For awards granted on or before December 31, 2005, we applied the intrinsic value method of accounting for employee stock option awards. Under the intrinsic value method, compensation expense for employees was based on the difference, if any, between the fair value of our common stock and the exercise price of the option on the measurement date, which is the date of grant.

On August 11, 2005, as a result of an equity restructuring that resulted in a new measurement date for our outstanding options, we recorded \$5.6 million of deferred stock-based compensation expense on the balance sheets that we subsequently amortized and recognized as stock-based compensation expense over the vesting period of the underlying options. The deferred stock-based compensation relating to this equity restructuring was fully amortized as of December 31, 2009.

Effective January 1, 2006, we adopted authoritative accounting guidance for stock-based compensation, which requires us to measure the cost of employee services received in exchange for stock-based awards based on the grant date fair value of the award. We adopted the guidance using the prospective transition method. Under the prospective transition method, compensation cost for stock-based awards granted prior to

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PACIFIC BIOSCIENCES OF CALIFORNIA, INC.

(A development stage enterprise)

Notes to Consolidated Financial Statements (Continued)

2. Summary of Significant Accounting Policies (Continued)

December 31, 2005 continue to be recorded based on the intrinsic value method. Compensation cost for all stock-based awards granted or modified subsequent to adoption is recorded based on the estimated grant date fair value and recognized as expense over the requisite service period of the grant, which is generally the vesting period.

We determine the grant date fair value of stock options using the Black-Scholes option pricing model. The use of the Black-Scholes option pricing model requires assumptions regarding a number of highly complex and subjective variables. These variables include, but are not limited to, future expected common stock price volatility over the term of the option awards, as well as projected employee option exercise behavior (expected period between stock option vesting date and stock option exercise date), risk-free interest rates and expected dividends.

Stock-based compensation expense recognized at fair value reflects the impact of estimated forfeitures. Future forfeitures are estimated at the date of grant and revised in subsequent periods if actual forfeitures differ from those estimates.

Convertible Preferred Stock Warrants

Prior to our IPO in October 2010, we accounted for freestanding warrants to purchase shares of our convertible preferred stock at fair value on the balance sheet because we may have been obligated to redeem these warrants at some point in the future. The warrants were subject to remeasurement at each balance sheet date with changes in fair value recognized as other expense, net in the consolidated statement of operations. We continued to adjust the liability for changes in fair value until our IPO, at which time all unexercised warrants automatically converted into warrants to purchase common stock and the warrant liability was reclassified to additional paid-in capital.

Segments

We operate as a single segment, use one measurement of financial performance and do not segregate our business for internal reporting.

Other Comprehensive Income (loss)

Other comprehensive income (loss) is comprised of unrealized gains (losses) on our investment securities. Total comprehensive income (loss) for all periods presented has been disclosed in the consolidated statements of stockholders' equity (deficit).

Recent Accounting Pronouncements

During the fourth quarter of 2010, we adopted the new disclosure guidance related to the credit quality of financing receivables and the allowance for credit losses. This guidance requires companies to provide more information about the credit quality of their financing receivables in the disclosures to financial statements including, but not limited to, significant purchases and sales of financing receivables, aging information and credit quality indicators. The adoption of this accounting guidance did not have a significant impact on our consolidated financial statements.

In October 2009, the FASB issued an accounting standards update that provides application guidance on whether multiple deliverables exist, how the deliverables should be separated and how the consideration should

Table of Contents**PACIFIC BIOSCIENCES OF CALIFORNIA, INC.****(A development stage enterprise)****Notes to Consolidated Financial Statements (Continued)****2. Summary of Significant Accounting Policies (Continued)**

be allocated to one or more units of accounting. This update establishes a selling price hierarchy for determining the selling price of a deliverable. The selling price used for each deliverable will be based on vendor-specific objective evidence, if available, third-party evidence if vendor-specific objective evidence is not available, or estimated selling price if neither vendor-specific nor third-party evidence is available. We will be required to apply this guidance prospectively for revenue arrangements entered into or materially modified after January 1, 2011. Our revenue to date has been limited to government grant revenue and no revenue has been recognized from the sale of our products. Therefore, adoption of this guidance is not expected to have a material impact on our financial statements.

3. Investments

The following table summarizes our investments as of December 31, 2010 and 2009 (in thousands):

	Amortized Cost	As of December 31, 2010 Gross unrealized gains	Gross unrealized losses	Fair Value
Commercial Paper	\$ 59,572	\$ 1	\$	\$ 59,573
Corporate Debt Securities	49,987	11	(28)	49,970
U.S. Government and Agency Securities	47,146	3	(8)	47,141
	\$ 156,705	\$ 15	\$ (36)	\$ 156,684
	Amortized Cost	As of December 31, 2009 Gross unrealized gains	Gross unrealized losses	Fair Value
Corporate Debt Securities	\$ 3,502	\$ 2	\$ (1)	\$ 3,503
	\$ 3,502	\$ 2	\$ (1)	\$ 3,503

4. Balance Sheet Components

In 2010, we began recording inventory to our consolidated balance sheet. As of December 31, 2010 our inventory consisted of the following (in thousands).

	December 31, 2010
Purchased materials	\$ 4,051
Work in Process	2,813

\$ 6,864

Table of Contents**PACIFIC BIOSCIENCES OF CALIFORNIA, INC.****(A development stage enterprise)****Notes to Consolidated Financial Statements (Continued)****4. Balance Sheet Components (Continued)**

As of December 31, 2010 and 2009, our property and equipment, net consisted of the following components (in thousands):

	December 31,	
	2010	2009
Building	\$ 1,160	\$
Laboratory equipment and machinery	10,998	10,307
Leasehold improvements	7,130	1,761
Computer equipment	3,033	1,928
Software	1,709	1,324
Furniture and fixtures	801	522
Construction in progress	8	619
	24,839	16,461
Less: Accumulated depreciation	(12,528)	(9,319)
Property and equipment, net	\$ 12,311	\$ 7,142

Depreciation expense during 2010, 2009, 2008, and for the period from July 14, 2000, the date of inception, to December 31, 2010, was \$5.2 million, \$4.1 million, \$3.0 million and \$15.6 million, respectively.

During December 2009, we entered into a lease agreement for a manufacturing and office facility, and in 2010 commenced renovations specific to our needs and operating requirements, including improvements and modifications to the facility's structure and principal operating systems. Pursuant to GAAP, this direct involvement renders us the owner of the facility for accounting purposes. Accordingly, upon commencement of construction activities, we recorded \$1.2 million for the fair value of the facility within property and equipment, net with a corresponding liability recorded to facility financing obligation.

In addition, pursuant to the terms of the lease arrangement, the landlord provided incentives to fund aspects of the construction project totaling \$1.8 million. The tenant improvement allowances afforded by the landlord are reflected on the balance sheet as a component of property and equipment. As we account for the leased facility as if we are the owner of the facility, we depreciate the assets over their expected useful lives.

As of December 31, 2010 and 2009, our accrued expenses and other current liabilities consisted of the following (in thousands):

	December 31,	December 31,
	2010	2009
Salaries and benefits	\$ 5,494	\$ 1,785
Professional services	659	358
Short-term portion of deferred rent	573	
Other	1,268	498

\$ 7,994 \$ 2,641

Table of Contents**PACIFIC BIOSCIENCES OF CALIFORNIA, INC.****(A development stage enterprise)****Notes to Consolidated Financial Statements (Continued)****5. Facility Financing and Debt Obligations***Facility Financing Obligation*

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

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

Based on the allocation of payments, the facility financing obligation bears an implied interest rate of 9.0%. During 2010, we recognized \$0.2 million of interest expense in our consolidated statement of operations relating to the facility financing obligation.

As of December 31, 2010, the future minimum payments due under the facility financing obligation were as follows (in thousands):

	Financing obligation
2011	\$ 397
2012	415
2013	433
2014	452
2015	473
Total Payments	2,170
Less amount representing interest	(1,284)
	886
Property reverting to landlord	2,151
Present value of obligation	3,037
Less current portion of obligation	(110)
Long-term portion of obligation	\$ 2,927

6. Commitments and Contingencies*Operating Lease Commitment*

As of December 31, 2010 we have noncancelable operating lease agreements for research and development, office, manufacturing and training facilities in Menlo Park, California that expire at various dates, with the latest expiration in December 2015. During 2010, we continued the expansion of our manufacturing and office space and renegotiated certain lease agreements to extend expiration dates. In December 2010, we

entered into three new leases for approximately 89,800 additional square feet which we intend to occupy in 2011.

Table of Contents**PACIFIC BIOSCIENCES OF CALIFORNIA, INC.****(A development stage enterprise)****Notes to Consolidated Financial Statements (Continued)****6. Commitments and Contingencies (Continued)**

Rent expense for 2010, 2009, 2008, and, cumulatively, for the period from July 14, 2000, the date of inception, to December 31, 2010, was \$2.1 million, \$1.4 million, \$1.1 million, and \$5.7 million, respectively. We are also required to pay our share of operating expenses with respect to the facilities in which we operate.

As of December 31, 2010, the future annual minimum lease payments under all noncancelable operating leases with an initial term in excess of one year are as follows (in thousands):

Years ending December 31:	Amount
2011	\$ 2,637
2012	3,077
2013	3,166
2014	3,256
2015	3,347
Thereafter	
Total minimum lease payments	\$ 15,483

Patent Agreement

During 2007, we entered into an agreement to purchase certain patents. The purchase agreement required a payment upfront of \$1.5 million and an additional \$0.5 million to be paid on the first and second anniversaries of the effective date. Payments for the years ended December 31, 2009 and 2008 and, cumulatively, for the period from July 14, 2000, the date of inception, to December 31, 2010 were \$0.5 million, \$0.5 million and \$2.5 million, respectively, and were expensed as incurred.

License Agreements

We have entered into four cancelable license agreements, as amended, with third parties for certain patent rights and technology. Under the terms of these agreements, we may be obligated to pay minimum royalty and license maintenance fees. License and maintenance fees for 2010, 2009 and 2008 and, cumulatively, for the period from July 14, 2000, our date of inception, to December 31, 2010, was \$0.3 million, \$0.2 million, \$0.1 million, and \$0.7 million, respectively. Pursuant to the terms of the agreements, future license maintenance fees and minimum royalty payments amount to \$0.4 million for each of 2011, 2012 and 2013 and thereafter.

Upon commercialization of products including the licensed technologies, we may be obligated to pay certain milestone fees of up to \$80,000. In addition, upon commercialization of products incorporating a technology provided under one license agreement, the amounts owed by us under that license decrease by \$5,000 in the first year following commercialization, return to the pre-commercialization amounts for the second year following commercialization, increase by \$10,000 the third year and by \$25,000 the fourth year following commercialization of products incorporating that licensed technology.

Contingencies

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

Table of Contents**PACIFIC BIOSCIENCES OF CALIFORNIA, INC.****(A development stage enterprise)****Notes to Consolidated Financial Statements (Continued)****6. Commitments and Contingencies (Continued)**

On August 27, 2010, we were named as a defendant in a complaint filed by Helicos Biosciences Corporation, or Helicos, alleging infringement of patents owned and in licensed by the plaintiffs. Helicos seeks a permanent injunction enjoining us from further infringement of the asserted patents, and unspecified monetary damages. On October 22, 2010, Helicos filed an amended complaint naming additional defendants in the lawsuit. On November 8, 2010, we filed our answer to Helicos' complaint denying Helicos' allegations, asserting affirmative defenses of noninfringement, invalidity and unenforceability of the claims of the patents in suit, and asserting counterclaims for declaratory judgment that our products do not infringe the claims of the patents in suit, and that those claims are invalid and unenforceable.

Despite our defenses and counterclaims, we cannot guarantee any outcome of this lawsuit. An estimate of the possible loss or possible range of loss associated with the resolution of this contingency cannot be provided with certainty or confidence, and therefore no estimate is provided and we have not recorded a liability.

Indemnification

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

We entered into indemnification agreements with our directors and officers that may require us to indemnify our directors and officers against liabilities that may arise by reason of their status or service as directors or officers, other than liabilities arising from willful misconduct of the individual. No liability associated with such indemnifications has been recorded at December 31, 2010.

7. Income Taxes

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

	Years Ended December 31,		
	2010	2009	2008
Statutory tax rate	(35.0)%	(34.0)%	(34.0)%
State tax rate, net of federal benefit	(5.7)	(5.8)	(5.8)
Stock-based compensation	1.6	1.0	1.3
Federal R&D credit	(2.0)	(2.6)	(2.8)
CA R&D credit	(1.1)	(1.8)	(1.9)
Other	0.2	0.3	0.4
Change in valuation allowance	43.5	42.9	42.5
Change of implied statutory tax rate to prior years	(1.5)	0.0	0.3
Effective income tax rate	0.0%	0.0%	0.0%

Table of Contents**PACIFIC BIOSCIENCES OF CALIFORNIA, INC.****(A development stage enterprise)****Notes to Consolidated Financial Statements (Continued)****7. Income Taxes (Continued)**

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

	December 31,	
	2010	2009
Net operating loss carryforwards	\$ 117,031	\$ 60,503
Research and development credits	12,391	7,568
Depreciation	1,342	2,272
Accruals and reserves	4,282	3,665
	135,046	74,008
Less: Valuation allowance	(135,046)	(74,008)
Net deferred tax assets	\$	\$

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

Recognition of deferred tax assets is appropriate when realization of such assets is more likely than not. Based upon the weight of available evidence, we believe it is more likely than not that the net deferred tax assets will not be fully realizable. Accordingly, we have provided a full valuation allowance against our net deferred tax assets as of December 31, 2010.

As of December 31, 2010, we had federal and state net operating loss carryforwards of approximately \$289.6 million and \$286.3 million, respectively, available to reduce future taxable income, if any.

The federal net operating loss carryforward begins expiring in 2025, and the state net operating loss carryforward begins expiring in 2015.

We also had federal and California state research and development credit carryforwards of approximately \$11.0 million and \$10.2 million, respectively, as of December 31, 2010. The federal credits will expire starting 2025 if not utilized. The California tax credits can be carried forward indefinitely.

Tax attributes related to stock option windfall deductions are not recorded until they result in a reduction of cash tax payable. Our federal and state net operating losses from windfall deductions were excluded from our deferred tax asset balance as of December 31, 2010. The benefit of the federal and state net operating loss deferred tax assets of \$0.6 million and \$0.1 million, respective, will be recorded to additional paid-in capital when they reduce cash tax payable.

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

Table of Contents**PACIFIC BIOSCIENCES OF CALIFORNIA, INC.****(A development stage enterprise)****Notes to Consolidated Financial Statements (Continued)****7. Income Taxes (Continued)**

Effective January 1, 2007, we adopted the provisions of the Financial Accounting Standard Board, or FASB, Accounting Standards Codification, or ASC, Topic 740-10, Accounting for Uncertainty in Income Taxes. The cumulative effect of adoption resulted in no adjustment of accumulated deficit as of January 1, 2007. As of December 31, 2010, our total unrecognized tax benefit was \$6.4 million, of which none of the tax benefit, if recognized, would affect the effective income tax rate due to the valuation allowance that currently offsets deferred tax assets. We do not anticipate the total amount of unrecognized income tax benefits to significantly increase or decrease in the next 12 months.

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

Balance as of December 31, 2008	\$ 1,912
Increase in balance related to tax positions taken during 2009	2,025
Balance as of December 31, 2009	3,937
Increase in balance related to tax positions taken in prior year	198
Increase in balance related to tax positions taken during current year	2,222
Balance as of December 31, 2010	\$ 6,357

Our practice is to recognize interest and/or penalties related to income tax matters in income tax expense. As of December 31, 2010 and 2009, we had no accrued interest or penalties due to our net operating losses available to offset any tax adjustment. We file U.S. federal and various state income tax returns. For U.S. federal and state income tax purposes, the statute of limitation currently remains open for the years ending December 31, 2007 to present and December 31, 2006 to present, respectively. In addition, all of the net operating losses and research and development credit carryforwards that may be utilized in future years may be subject to examination. We are not currently under examination by tax authorities in any jurisdiction.

8. Convertible Preferred Stock

As of December 31, 2010, there were no shares of convertible preferred stock issued or outstanding as all shares of preferred stock converted to shares of common stock upon completion of the IPO.

As of December 31, 2009, our convertible preferred stock consisted of the following (dollars in thousands):

Series	Shares		Proceeds Net of Issuance Costs	Conversion to Junior Preferred Stock	Carrying Amount	Liquidation Value
	Authorized	Outstanding				
A	5,405,992	5,405,992	\$ 5,237	\$	\$ 5,237	\$ 5,406
B	3,530,768	3,500,000	4,495		4,495	4,550
C	5,342,197	5,322,396	10,669		10,669	10,751

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D	12,525,000	12,500,000	49,812		49,812	50,000
E	27,857,195	26,866,790	187,841		187,841	188,068
Junior Preferred Stock	61,395,230	6,506,160	281	10,766	11,047	6,506
	116,056,382	60,101,338	\$ 258,335	\$ 10,766	\$ 269,101	\$ 265,281

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PACIFIC BIOSCIENCES OF CALIFORNIA, INC.

(A development stage enterprise)

Notes to Consolidated Financial Statements (Continued)

8. Convertible Preferred Stock and Junior Preferred Stock (Continued)

During June and July 2010, we issued an aggregate of 14,265,782 shares of Series F convertible preferred stock at \$7.63 per share and received proceeds of \$106.1 million, net of issuance costs of \$2.9 million, bringing our aggregate preferred stock outstanding at the time of the IPO to 74,367,120 shares. Each share of convertible preferred stock converted on a two-for one basis into common stock upon the closing of our IPO declared effective by the SEC on October 26, 2010.

Warrants to Purchase Convertible Preferred Stock

In connection with loan and security agreements entered into in 2004 and 2006 which have since been fully repaid, we issued 50,569 warrants to purchase convertible preferred stock. The fair value of the warrants was estimated using the Black-Scholes valuation model at the dates of issuance and recorded as debt issuance costs that were amortized to interest expense over the contractual life of 7 years. The fair value of the warrants outstanding was recorded as a liability and revalued each subsequent reporting period with the resulting gains and losses recorded in other expense, net. In accordance with these revaluations, we recorded expense (income) of approximately \$100,000, \$84,000 and \$(9,000) for the years ended December 31, 2010, 2009 and 2008. For the cumulative period from July 14, 2000 (date of inception) to December 31, 2010, approximately \$0.3 million was recorded as expense as a result of the revaluation.

We continued to adjust the liability for changes in fair value until the completion of our IPO, at which time all unexercised warrants converted into warrants to purchase 25,282 shares of common stock and the liability was reclassified to stockholders equity. On November 1, 2010, 15,384 warrants to purchase common stock were exercised.

9. Common Stock

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

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

Early Exercise of Employee Options

Stock options granted under the 2005 Stock Plan provide employee option holders the right to exercise unvested options in exchange for restricted common stock. The stock option tables in Note 11 include unvested shares which amounted to 169,176, 59,145 and 155,364 at December 31, 2010, 2009, and 2008, respectively, which are subject to a repurchase right held by us at the original issuance price in the event the optionees' employment is terminated either voluntarily or involuntarily. Generally, this right lapses as to 25% on the first anniversary of the vesting start date and in 36 equal monthly amounts thereafter.

These repurchase terms are considered to be a forfeiture provision and do not result in variable accounting. The restricted shares issued upon early exercise of stock options are legally issued and outstanding. However, these restricted shares are only deemed outstanding for basic earnings per share computation purposes upon the respective repurchase rights lapsing. We treat cash received from employees for the exercise of unvested options as a refundable deposit shown as a liability in our balance sheets. As of December 31, 2010, 2009, and 2008, we

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PACIFIC BIOSCIENCES OF CALIFORNIA, INC.

(A development stage enterprise)

Notes to Consolidated Financial Statements (Continued)

9. Common Stock (Continued)

included cash received for early exercise of options of \$0.8 million, \$0.2 million and \$0.2 million, respectively, in accrued liabilities. Amounts from accrued liabilities are transferred into common stock and additional paid-in capital as the shares vest.

10. Stock Option Plans

As of December 31, 2010, we had two active equity compensation plans, the 2010 Equity Incentive Plan, or 2010 Plan, and the 2010 Outside Director Equity Incentive Plan, or 2010 Director Plan, both of which we adopted upon the effectiveness of our IPO during October 2010. Prior to the adoption of these plans, we granted options pursuant to the 2004 Equity Incentive Plan, through August 2005, and the 2005 Stock Plan, through October 2010. Upon termination of the predecessor plans, the shares available for grant at the time of termination, and shares subsequently returned to the plans upon forfeiture or option termination, were transferred to the successor plan in effect at the time of share return.

2010 Equity Incentive Plan

Stock options granted under the 2010 Plan may be either ISOs or NSOs. ISOs may be granted only to employees. NSOs may be granted to employees, consultants and directors. Stock options under the 2010 Plan may be granted with a term of up to ten years and at prices no less than the fair market value of our common stock on the date of grant. To date, stock options granted generally vest over four years and vest at a rate of 25% upon the first anniversary of the vesting commencement date and 1/48th per month thereafter. As of December 31, 2010 we had reserved 2,500,000 shares of common stock for issuance under the 2010 Plan.

The remaining common stock available for issuance under the 2005 Plan were made available for future grant under the 2010 Plan. Outstanding options under the 2005 Plan that expire or are canceled without having been exercised in full or are repurchased or forfeited will be available for future issuance under the 2010 Plan. We issue new shares of common stock upon exercise of stock options.

2010 Outside Director Equity Incentive Plan

Stock options granted under the 2010 Director Plan provide for the grant of NSOs. Stock options under the 2010 Plan may be granted with a term of up to ten years and at prices no less than the fair market value of our common stock on the date of grant. To date, stock options granted generally vest over three years and vest at a rate of one-third upon the first anniversary of the vesting commencement date and 1/36th per month thereafter. As of December 31, 2010 we had reserved 500,000 shares of common stock for issuance under the 2010 Director Plan.

Table of Contents**PACIFIC BIOSCIENCES OF CALIFORNIA, INC.**

(A development stage enterprise)

Notes to Consolidated Financial Statements (Continued)**10. Stock Option Plans (Continued)***Stock Options*

The following table summarizes stock option activity for all stock option plans:

	Common Stock Options Outstanding				Weighted average exercise price
	Shares available for grant	Number of shares	Exercise price		
Options granted		1,379,000	\$ 0.20	0.26	\$ 0.21
Options exercised		(845,375)	\$	0.20	\$ 0.20
Balances, December 31, 2004		533,625	\$ 0.20	0.26	\$ 0.22
Additional shares reserved	766,748				
Options granted	(770,726)	770,726	\$ 0.26	0.70	\$ 0.54
Options exercised		(506,699)	\$ 0.20	0.26	\$ 0.23
Options canceled	41,822	(41,822)	\$ 0.20	0.26	\$ 0.21
Balances, December 31, 2005	37,844	755,830	\$ 0.20 - 0.70		\$ 0.53
Additional shares reserved	1,226,735				
Options granted	(772,550)	772,550	\$ 0.70 - 0.70		\$ 0.70
Options exercised		(163,497)	\$ 0.20	0.70	\$ 0.62
Options repurchased and added back into pool	121,132				
Options canceled	91,376	(91,376)	\$ 0.26	0.70	\$ 0.38
Balances, December 31, 2006	704,537	1,273,507	\$ 0.20	0.70	\$ 0.63
Additional shares reserved	1,550,000				
Options granted	(2,222,701)	2,222,701	\$ 1.96	1.96	\$ 1.96
Options exercised		(159,634)	\$ 0.26	1.96	\$ 1.08
Options repurchased and added back into pool	7,032				
Options canceled	201,209	(201,209)	\$ 0.70	1.96	\$ 1.13
Balances, December 31, 2007	240,077	3,135,365	\$ 0.20	1.96	\$ 1.52
Additional shares reserved	2,903,923				
Options granted	(2,274,127)	2,274,127	\$ 2.52	6.96	\$ 5.25
Options exercised		(343,095)	\$ 0.20	6.96	\$ 1.45
Options canceled	106,649	(106,649)	\$ 0.70	6.96	\$ 2.18

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Balances, December 31, 2008	976,522	4,959,748	\$ 0.20	6.96	\$ 3.22
Additional shares reserved	2,705,678				
Options granted	(1,786,251)	1,786,251	\$ 3.86	8.50	\$ 5.66
Options exercised		(89,241)	\$ 0.26	6.96	\$ 3.50
Options repurchased and added back into pool	5,177				
Options canceled	81,923	(81,923)	\$ 1.96	6.96	\$ 5.35
Balances, December 31, 2009	1,983,049	6,574,835	\$ 0.20 - 8.50		\$ 3.85
Additional shares reserved	5,500,000				
Options granted	(4,139,143)	4,139,143	\$ 8.50 - 16.00		\$ 10.85
Options exercised		(606,963)	\$ 0.70	10.84	\$ 2.86
Options canceled	293,642	(293,642)	\$ 1.96	13.42	\$ 6.84
Balances, December 31, 2010	3,637,548	9,813,373	\$ 0.20 - 16.00		\$ 6.78

Table of Contents**PACIFIC BIOSCIENCES OF CALIFORNIA, INC.**

(A development stage enterprise)

Notes to Consolidated Financial Statements (Continued)**10. Stock Option Plans (Continued)**

The following table summarizes information with respect to stock options outstanding and exercisable under the plans at December 31, 2010 (dollars in thousands, except per share values):

Exercise price	Number outstanding	Options outstanding			Options vested and exercisable		
		Weighted average contractual life (Years)	Weighted average exercise price	Aggregate intrinsic value	Number vested	Weighted average exercise price	Aggregate intrinsic value
\$0.22 3.20	2,950,395	6.22	\$ 1.75		2,419,960	\$ 1.65	
\$3.21 6.40	1,207,072	8.32	\$ 4.61		495,046	\$ 4.55	
\$6.41 8.00	1,239,901	7.69	\$ 6.96		665,034	\$ 6.96	
\$8.01 11.20	2,885,650	9.04	\$ 8.94		663,991	\$ 8.51	
\$11.21 14.40	1,101,896	9.65	\$ 13.15		729	\$ 12.74	
\$14.41 16.00	428,459	9.82	\$ 16.00			n/a	
	9,813,373		\$ 6.78	\$ 89,669	4,244,760	\$ 3.89	\$ 51,001

We have computed the aggregate intrinsic value amounts disclosed in the above table based upon the difference between the original exercise price of the options and our estimate of the deemed fair value of our common stock of \$15.91 per share at December 31, 2010.

The total intrinsic value of options exercised during the years ended December 31, 2010 and 2009 was \$6.0 million and \$0.3 million, respectively.

Stock-based Compensation

Stock-based compensation expense under the fair value method for options granted to employees and non-employees was allocated to research and development expense, sales, general and administrative expense as follows (in thousands):

	Years Ended December 31,			Period From
	2010	2009	2008	July 14, 2000 (Date of Inception) to December 31, 2010
Research and development	\$ 5,733	\$ 2,314	\$ 1,183	\$ 9,678
Sales, general and administrative	3,112	748	387	4,508
Total stock-based compensation expense	\$ 8,845	\$ 3,062	\$ 1,570	\$ 14,186

Employee Stock-based Compensation

During the years ended December 31, 2010, 2009 and 2008, we granted 4,126,393, 1,712,500 and 2,182,375 stock options, respectively, to employees with a weighted-average grant date fair value of \$5.49, \$2.58 and \$2.92 per share, respectively. As of December 31, 2010 there was unrecognized compensation costs of \$23.2 million related to these stock options. We expect to recognize those costs over a weighted-average period of 3.2 years as of December 31, 2010. Future option grants will increase the amount of compensation expense to be recorded in these periods.

Table of Contents**PACIFIC BIOSCIENCES OF CALIFORNIA, INC.****(A development stage enterprise)****Notes to Consolidated Financial Statements (Continued)****10. Stock Option Plans (Continued)**

We estimated the fair value of employee stock options using the Black-Scholes option pricing model. The fair value of employee stock options is being amortized on a straight-line basis over the requisite service period of the awards. The fair value of employee stock options was estimated using the following assumptions:

	Years ended December 31,		
	2010	2009	2008
Expected term	6.0 years	5.7 years	7.0 years
Expected volatility	46 - 55%	46 - 48%	50 - 52%
Risk-free interest rate	1.6 - 2.7%	1.8 - 3.0%	2.8 - 3.5%
Dividend yield			

Expected term Expected term represents the period that our stock-based awards are expected to be outstanding. Our assumptions about the expected term have been on our historic cancellation and exercise experience and trends as well as our expectations for future periods.

Expected volatility We do not have sufficient trading history to use the volatility of our own common stock for establishing expected volatility. Therefore, we based our expected volatility on the historical stock volatilities of several publicly listed comparable companies over a period equal to the expected terms of the options, as.

Risk-free interest rate The risk-free interest rate is based on the U.S. Treasury yield curve in effect at the time of grant for zero coupon U.S. Treasury notes with maturities approximately equal to the option's expected term.

Dividend yield We have never paid dividends and do not expect to pay dividends for the foreseeable future.

Fair value of common stock The fair values of the common stock underlying stock options granted through September 2010 were estimated by our board of directors, which intended all options granted to be exercisable at a price per share not less than the per share fair value of our common stock underlying those options on the date of grant. The fair value of the shares of common stock underlying the stock options has historically been the responsibility of and determined by our board of directors. Because there has been no public market for our common stock, our board of directors has determined fair value of the common stock at the time of grant of the option by considering a number of objective and subjective factors including independent third-party valuations of our common stock, sales of convertible preferred stock to unrelated third parties, operating and financial performance, the lack of liquidity of capital stock and general and industry specific economic outlook, amongst other factors. The fair value of the underlying common stock shall be determined by our board of directors until such time as our common stock is listed on an established stock exchange or national market system.

Our common stock became publicly listed upon our IPO at which time options granted are issued at a price equal to the closing price on the date of grant.

Forfeiture rate We estimate our forfeiture rate based on an analysis of our actual forfeitures and will continue to evaluate the adequacy of the forfeiture rate based on actual forfeiture experience, analysis of

Table of Contents**PACIFIC BIOSCIENCES OF CALIFORNIA, INC.****(A development stage enterprise)****Notes to Consolidated Financial Statements (Continued)****10. Stock Option Plans (Continued)**

employee turnover behavior and other factors. The impact from a forfeiture rate adjustment will be recognized in full in the period of adjustment, and if the actual number of future forfeitures differs from that estimated, we may be required to record adjustments to stock-based compensation expense in future periods.

Each of the inputs discussed above is subjective and generally requires significant management and director judgment to determine.

Stock-based Compensation Associated with Junior Preferred Stock

In connection with our equity restructuring in 2005 in which all authorized and issued shares of common stock were converted into shares of junior preferred stock, all outstanding options to purchase common stock were converted into options to purchase junior preferred stock. We recorded deferred stock-based compensation of \$5.6 million in connection with the exchange of common stock options for junior preferred stock options which was fully amortized during 2009 as all the options became fully vested. As a result of a repricing which occurred in 2005, we applied variable accounting to the junior preferred stock options resulting in additional stock-based compensation of \$0.8 million, \$0.5 million, and \$0.1 million for the years ended December 31, 2010, 2009 and 2008, respectively.

Options Granted to Non-employees

During the years ended December 31, 2010, 2009 and 2008 we granted options to purchase 12,750, 73,750 and 95,750 shares of common stock, respectively, to non-employees at exercise prices ranging from \$1.96 to \$12.74 per share.

Stock-based compensation expense will fluctuate as the estimated fair value of the common stock fluctuates over the vesting period. In connection with the grant of stock options to non-employees, we recognized stock-based compensation expense of \$1.0 million, \$0.4 million, \$0.3 million and \$2.0 million, for the years ended December 31, 2010, 2009 and 2008 and the period from July 14, 2000, the date of inception, to December 31, 2010, respectively.

Stock-based compensation expense related to stock options granted to non-employees is recognized as the stock options are earned. We believe that the estimated fair value of the stock options is more readily measurable than the fair value of the services rendered. The fair value of the stock options granted to non-employees is calculated at each reporting date using the Black-Scholes option pricing model using the following assumptions:

	Years ended December 31,					
	2010		2009		2008	
Contractual life	10 years		10 years		10 years	
Expected volatility	60% - 75%		75%		75%	
Risk-free interest rate	3.3	3.9%	2.8	3.7%	2.4	4.1%
Dividend yield						

Table of Contents**PACIFIC BIOSCIENCES OF CALIFORNIA, INC.**

(A development stage enterprise)

Notes to Consolidated Financial Statements (Continued)**10. Stock Option Plans (Continued)***Shares Reserved for Future Issuance*

As of December 31, 2010 and 2009 we had reserved shares of Common Stock for issuance as follows:

	December 31, 2010	December 31, 2009
Conversion of Convertible Preferred Stock		30,050,669
Exercise of Options	13,450,922	8,610,959
Exercise of warrants	9,898	25,282
	13,460,820	38,686,910

11. Net Loss Per Share

We calculate basic net loss per share by dividing the net loss by the weighted-average number of unrestricted common shares outstanding for the period, without consideration of potentially dilutive securities. Diluted net loss per share is computed by dividing the net loss by the weighted-average number of unrestricted common shares and potentially dilutive securities outstanding for the period, determined using the treasury-stock method and the as if converted method. For purposes of this calculation, convertible preferred stock, stock options and common stock subject to repurchase, and warrants are considered to be potentially dilutive securities and are only included in the calculation of diluted net loss per share when their effect is dilutive.

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

	Years Ended December 31,		
	2010	2009	2008
Net loss per share:			
Numerator			
Net loss	\$ (140,166)	\$ (87,703)	\$ (43,754)
Denominator:			
Weighted average shares of common stock outstanding	10,024,347	601,512	455,964
Less: Shares of common stock subject to repurchase	(85,936)	(94,647)	(129,009)
Weighted average shares used in computation of basic and diluted net loss per share	9,938,411	506,865	326,955
Basic and diluted net loss per share	\$ (14.10)	\$ (173.03)	\$ (133.82)

Table of Contents**PACIFIC BIOSCIENCES OF CALIFORNIA, INC.**

(A development stage enterprise)

Notes to Consolidated Financial Statements (Continued)**11. Net Loss Per Share (Continued)**

The following convertible preferred stock, options outstanding, common stock subject to repurchase, and warrants to purchase common stock were excluded from the computation of diluted net loss per share for the periods presented because including them would have had an anti-dilutive effect:

	Years Ended December 31,		
	2010	2009	2008
Convertible Preferred Stock (on an as if converted basis)		30,050,669	25,183,728
Options outstanding	9,813,373	6,574,835	4,959,748
Common Stock subject to repurchase	169,176	59,145	155,364
Warrants to purchase Common Stock	9,898	25,282	25,282

12. Employee Benefit and Employee Stock Purchase Plan*Retirement Plans*

During 2005, we established a 401(k) Plan to provide tax deferred salary deductions for all eligible employees. Participants may make voluntary contributions to the 401(k) Plan up to 90% of their eligible compensation, limited by certain Internal Revenue Service restrictions. We do not match employee contributions.

Employee Stock Purchase Plan

Upon the effectiveness of our IPO in October 2010, we adopted the 2010 Employee Stock Purchase Plan, or ESPP. We reserved a total of 750,000 shares of common stock for issuance under the ESPP. We issue new shares of common stock upon the purchase of the option. Our ESPP permits eligible employees to purchase common stock at a discount through payroll deductions during defined offering periods. Each offering period will generally consist of four purchase periods, each purchase period being approximately six months. The price at which the stock is purchased is equal to the lower of 85% of the fair market value of the common stock at the beginning of an offering period or at the end of a purchase period. For the year ended December 31, 2010, no shares of common stock were purchased under the Plan.

Under the ESPP, rights to purchase shares are generally granted during the first and third quarter of each year. The fair value of rights granted under the ESPP was estimated at the date of grant using the Black-Scholes option-pricing model. The estimated weighted average value of rights granted under the Employee Stock Purchase Plan during 2010 was \$6.34. The fair value of rights granted during 2010 were estimated at the date of grant using the following weighted-average assumptions:

	December 31, 2010
Expected term	1.3 years
Expected volatility	55%
Risk-free interest rate	0.3%
Expected Dividend yield	

Expected term Expected term represents the period that awards are expected to be outstanding and correlate to the respective offering periods of the rights granted.

Table of Contents**PACIFIC BIOSCIENCES OF CALIFORNIA, INC.****(A development stage enterprise)****Notes to Consolidated Financial Statements (Continued)****12. Employee Benefit and Employee Stock Purchase Plan (Continued)**

Expected volatility The expected volatility was based on the historical stock volatilities of several publicly listed comparable companies over a period equal to the expected terms of the options, as we do not have any trading history to use the volatility of our own common stock.

Risk-free interest rate The risk-free interest rate is based on the U.S. Treasury yield curve in effect at the time of grant for zero coupon U.S. Treasury notes with maturities approximately equal to the award's expected term.

Expected dividend yield We have never paid dividends and do not expect to pay dividends.

13. Quarterly Financial Data (unaudited)

The following table summarizes the unaudited quarterly financial data for the last two fiscal years.

(In thousands, except per share data)	Fiscal 2010 Quarter Ended			
	March 31,	June 30,	September 30,	December 31,
Total operating expenses	\$ 30,819	\$ 33,304	\$ 40,916	\$ 36,869
Loss from operations	(30,274)	(32,675)	(40,696)	(36,589)
Net loss	(30,325)	(32,714)	(40,708)	(36,419)
Basic and diluted net loss per share of Common Stock	\$ (48.97)	\$ (49.76)	\$ (39.70)	\$ (0.97)

	Fiscal 2009 Quarter Ended			
	March 31,	June 30,	September 30,	December 31,
Total operating expenses	\$ 16,348	\$ 19,080	\$ 24,568	\$ 28,209
Loss from operations	(16,348)	(19,080)	(24,568)	(28,074)
Net loss	(16,099)	(19,012)	(24,529)	(28,063)
Basic and diluted net loss per share of Common Stock	\$ (34.95)	\$ (38.53)	\$ (46.74)	\$ (48.05)

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ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE.

None.

ITEM 9A. CONTROLS AND PROCEDURES.

Evaluation of Controls and Procedures

Our management, with the participation of our chief executive officer and our chief financial officer, evaluated the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) of the Exchange Act) as of the end of the period covered by this Annual Report on Form 10-K. Based on this evaluation, our chief executive officer and our chief financial officer concluded that our disclosure controls and procedures are designed at a reasonable assurance level and are effective to provide reasonable assurance that information required to be disclosed by us in the reports that we file or submit under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms and that such information is accumulated and communicated to our management, including our chief executive officer and our chief financial officer, as appropriate, to allow timely decisions regarding required disclosure.

Management's Annual Report on Internal Control Over Financial Reporting

This Annual Report on Form 10-K does not include a report of management's assessment regarding internal control over financial reporting or an attestation report of the Company's independent registered public accounting firm due to a transition period established by rules of the Securities and Exchange Commission for newly public companies.

Changes in Internal Control Over Financial Reporting

There were no changes in our internal control over financial reporting during our fourth fiscal quarter that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

ITEM 9B. OTHER INFORMATION

None.

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PART III

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE.

Information responsive to this item is incorporated herein by reference to our definitive proxy statement with respect to our 2011 Annual Meeting of Shareholders to be filed with the SEC within 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K.

ITEM 11. EXECUTIVE COMPENSATION.

Information responsive to this item is incorporated herein by reference to our definitive proxy statement with respect to our 2011 Annual Meeting of Shareholders to be filed with the SEC within 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K.

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

Information responsive to this item is incorporated herein by reference to our definitive proxy statement with respect to our 2011 Annual Meeting of Shareholders to be filed with the SEC within 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K.

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

Information responsive to this item is incorporated herein by reference to our definitive proxy statement with respect to our 2011 Annual Meeting of Shareholders to be filed with the SEC within 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K.

ITEM 14. PRINCIPAL ACCOUNTING FEES AND SERVICES.

Information responsive to this item is incorporated herein by reference to our definitive proxy statement with respect to our 2011 Annual Meeting of Shareholders to be filed with the SEC within 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K.

PART IV

ITEM 15. EXHIBITS, FINANCIAL STATEMENT SCHEDULES.

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

1. *Financial Statements*: See Index to Consolidated Financial Statements under Item 8 of this Annual Report on Form 10-K.
2. *Financial Statement Schedules*: All schedules are omitted because they are not required, are not applicable or the information is included in the consolidated financial statements or notes thereto.
3. *Exhibits*: We have filed, or incorporated by reference into this Annual Report on Form 10-K, the exhibits listed on the accompanying Exhibit Index immediately following the signature page of this Annual Report on Form 10-K.

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

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

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Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this Annual Report on Form 10-K to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Menlo Park, State of California, on March 23, 2011.

PACIFIC BIOSCIENCES OF CALIFORNIA, INC.

By: /s/ SUSAN K. BARNES
Susan K. Barnes

Senior Vice President and Chief Financial Officer

POWER OF ATTORNEY

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

Pursuant to the requirements of the Securities Act of 1933, this registration statement has been signed by the following persons in the capacities indicated below:

Signature	Title	Date
/s/ Hugh C. Martin Hugh C. Martin	Chairman, Chief Executive Officer and President	March 23, 2011
/s/ SUSAN K. BARNES Susan K. Barnes	Senior Vice President and Chief Financial Officer	March 23, 2011
/s/ Brian B. Dow Brian B. Dow	Vice President, Finance and Principal Accounting Officer	March 23, 2011
/s/ Brook Byers Brook Byers	Director	March 23, 2011
/s/ William W. Ericson William W. Ericson	Director	March 23, 2011
/s/ Michael Hunkapiller Michael Hunkapiller	Director	March 23, 2011

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/s/ Randall S. Livingston	Director	March 23, 2011
Randall S. Livingston		
/s/ Susan Siegel	Director	March 23, 2011
Susan Siegel		
/s/ David B. Singer	Director	March 23, 2011
David B. Singer		

Table of Contents**Exhibit Index**

Exhibit Number	Description	Incorporated by reference herein		
		Form	Exhibit No.	Filing Date
3.1	Amended and Restated Certificate of Incorporation			
3.2	Amended and Restated Bylaws			
4.1	Specimen Common Stock Certificate	S-1/A	4.1	October 1, 2010
4.2	Fifth Amended and Restated Investor Rights Agreement, dated June 16, 2010	S-1	4.2	August 16, 2010
10.1+	Form of Director and Executive Officer Indemnification Agreement	S-1	10.1	August 16, 2010
10.2+	2004 Equity Incentive Plan and forms of agreement thereunder	S-1	10.2	August 16, 2010
10.3+	2005 Stock Plan and forms of option agreements thereunder	S-1	10.3	August 16, 2010
10.4+	2010 Equity Incentive Plan and forms of option agreements thereunder	S-1	10.4	August 16, 2010
10.5+	2010 Employee Stock Purchase Plan and forms of agreement thereunder	S-1	10.5	August 16, 2010
10.6+	2010 Outside Director Equity Incentive Plan and forms of agreement thereunder	S-1	10.6	August 16, 2010
10.7	Collaboration Agreement by and between the Registrant and Gen-Probe Incorporated, dated as of June 15, 2010	S-1/A	10.7	October 22, 2010
10.8	Exclusive License Agreement by and between the Registrant and Cornell Research Foundation, Inc., dated as of February 1, 2004	S-1/A	10.8	October 22, 2010
10.9	License Agreement by and between the Registrant and GE Healthcare Bio-Sciences Corp., dated as of September 11, 2006	S-1/A	10.9	October 22, 2010
10.10	Exclusive License Agreement by and between the Registrant and Indiana University Research and Technology Corporation, dated May 15, 2005	S-1/A	10.10	October 19, 2010
10.11	Amended and Restated Lease Agreement by and between the Registrant and Menlo Business Park, LLC, dated as of December 17, 2007	S-1	10.11	August 16, 2010
10.12	Lease Agreement by and between the Registrant and Menlo Business Park LLC, dated August 14, 2009	S-1	10.12	August 16, 2010
10.13	Industrial Lease Agreement by and between the Registrant and AMB Property, L.P., dated December 10, 2009	S-1	10.13	August 16, 2010

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Exhibit Number	Description	Incorporated by reference herein		
		Form	Exhibit No.	Filing Date
10.14	Third Amendment to the December 10, 2009 Industrial Lease by and between the Registrant and AMB Property, L.P. dated December 29, 2010			
10.15	Industrial Lease Agreement by and between the Registrant and AMB Property, L.P., dated September 24, 2009	S-1	10.14	August 16, 2010
10.16	Third Amendment to the September 24, 2009 Industrial Lease by and between the Registrant and AMB Property, L.P. dated December 29, 2010			
10.17	First Amendment to the September 24, 2009 Industrial Lease Agreement by and between the Registrant and AMB Property, L.P., dated as of May 19, 2010	S-1	10.15	August 16, 2010
10.18	Industrial Lease Agreement by and between the Registrant and AMB Property, L.P., dated February 8, 2010	S-1	10.16	August 16, 2010
10.19	First Amendment to the February 8, 2010 Industrial Lease by and between the Registrant and AMB Property, L.P. dated December 29, 2010			
10.20	Lease by and between the Registrant and Willow Park Holding Company I, L.P. dated December 17, 2010			
10.21	Lease by and between the Registrant and AMB Property, L.P. dated December 17, 2010			
10.22	Lease by and between the Registrant and Willow Park Holding Company II, L.P. dated December 17, 2010			
10.23+	Employment Agreement by and between the registrant and Hugh Martin effective September 16, 2010	S-1/A	10.17	September 20, 2010
10.24+	Change in Control Severance Agreement by and between the registrant and Hugh Martin effective September 16, 2010	S-1/A	10.18	September 20, 2010
10.25+	Letter Relating to Employment Terms by and between the registrant and Susan K. Barnes effective September 15, 2010	S-1/A	10.19	September 20, 2010
10.26+	Change in Control Severance Agreement by and between the registrant and Susan K. Barnes effective September 9, 2010	S-1/A	10.20	September 20, 2010
10.27+	Letter Relating to Employment Terms by and between the registrant and Stephen Turner effective September 15, 2010	S-1/A	10.21	September 20, 2010
10.28+	Change in Control Severance Agreement by and between the registrant and Stephen Turner effective September 9, 2010	S-1/A	10.22	September 20, 2010

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Exhibit Number	Description	Incorporated by reference herein		
		Form	Exhibit No.	Filing Date
10.29+	Letter Relating to Employment Terms by and between the registrant and James Michael Phillips effective September 15, 2010	S-1/A	10.23	September 20, 2010
10.30+	Change in Control Severance Agreement by and between the registrant and James Michael Phillips effective September 9, 2010	S-1/A	10.24	September 20, 2010
23.1	Consent of PricewaterhouseCoopers LLP, Independent Registered Public Accounting Firm			
31.1	Certification of Chief Executive Officer pursuant to Exchange Act Rules 13a-14(a) and 15d-14(a), as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002			
31.2	Certification of Chief Financial Officer pursuant to Exchange Act Rules 13a-14(a) and 15d-14(a), as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002			
32.1	Certifications of Chief Executive Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002			
32.2	Certifications of Chief Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002			

- + Indicates management contract or compensatory plan
Confidential treatment has been requested for portions of this exhibit. These portions have been omitted from this Registration Statement and have been filed separately with the Securities and Exchange Commission.