

PACIFIC BIOSCIENCES OF CALIFORNIA INC
Form S-1/A
September 20, 2010
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As filed with the Securities and Exchange Commission on September 17, 2010

Registration No. 333-168858

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

AMENDMENT NO. 1 TO
FORM S-1

REGISTRATION STATEMENT UNDER THE SECURITIES ACT OF 1933

Pacific Biosciences of California, Inc.

(Exact name of Registrant as specified in its charter)

Delaware
*(State or other jurisdiction of
incorporation or organization)*

3826
*(Primary Standard Industrial
Classification Code Number)*
1380 Willow Road

16-1590339
*(I.R.S. Employer
Identification Number)*

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Menlo Park, CA 94025

(650) 521-8000

(Address, including zip code, and telephone number, including area code, of Registrant's principal executive offices)

Hugh C. Martin

Chief Executive Officer

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Approximate date of commencement of proposed sale to the public: As soon as practicable after this registration statement becomes effective.

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933 check the following box:

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

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

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

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

Large accelerated filer "

Accelerated filer "

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

Smaller reporting company "

The registrant hereby amends this registration statement on such date or dates as may be necessary to delay its effective date until the registrant shall file a further amendment which specifically states that this registration statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933 or until the registration statement shall become effective on such date as the Securities and Exchange Commission, acting pursuant to said Section 8(a), may determine.

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

Prospectus (Subject to Completion)

Issued September 17, 2010

Shares

Common Stock

This is the initial public offering of common stock of Pacific Biosciences of California, Inc. Prior to this offering, there has been no public market for our common stock. The initial public offering price of our common stock is expected to be between \$ and \$ per share.

We expect to apply for listing of our common stock on the NASDAQ Global Market under the symbol **PACB** .

	<i>Per share</i>	<i>Total</i>
Initial public offering price	\$	\$
Underwriting discounts and commissions	\$	\$
Proceeds to Pacific Biosciences, before expenses	\$	\$

We have granted the underwriters an option to purchase up to additional shares of common stock to cover over-allotments.

Investing in our common stock involves risks. See Risk Factors beginning on page 10.

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

The underwriters expect to deliver the shares on or about _____, 2010.

J.P.Morgan

Morgan Stanley

Deutsche Bank Securities

Piper Jaffray

, 2010

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We have not authorized anyone to provide any information other than that contained or incorporated by reference in this prospectus or in any free writing prospectus prepared by or on behalf of us or to which we have referred you. We take no responsibility for, and can provide no assurance as to the reliability of, any information that others may give you. This prospectus is an offer to sell only the shares offered hereby but only under circumstances and in jurisdictions where it is lawful to do so. The information contained in this prospectus is current only as of its date.

Through and including _____, 2010 (the 25th day after the date of this prospectus), all dealers effecting transactions in these securities, whether or not participating in this offering, may be required to deliver a prospectus. This is in addition to a dealer's obligation to deliver a prospectus when acting as an underwriter and with respect to an unsold allotment or subscription.

For investors outside the United States, neither we nor any of the underwriters have done anything that would permit this offering or possession or distribution of this prospectus in any jurisdiction where action for that purpose is required, other than the United States. If you are an investor outside the United States, you are required to inform yourselves about and to observe any restrictions relating to this offering and the distribution of this prospectus.

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PROSPECTUS SUMMARY

This summary highlights selected information appearing elsewhere in this prospectus and does not contain all the information you should consider before investing in our common stock. You should carefully read this prospectus in its entirety before investing in our common stock, including the section entitled Risk Factors, and our financial statements and related notes included elsewhere in this prospectus.

Overview

We develop, manufacture and market an integrated platform for genetic analysis. We have developed an approach to study the synthesis and regulation of deoxyribonucleic acid, or DNA. 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 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 research community with a new tool for investigating basic biochemical processes such as DNA synthesis. We believe 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, the PacBio RS. We believe that the PacBio RS, which uses our proprietary SMRT technology, maintains many of the key attributes of currently available sequencing technologies while solving many of the inherent limitations of previous technologies. Our system provides long readlengths, flexibility in experimental design, fast time to result and is designed to be easy to use. The PacBio RS consists of an instrument platform and the proprietary products necessary to run the platform, which we call consumables. Our proprietary consumables are currently comprised of our SMRT Cells and three chemical reagent kits. The system is designed to be integrated into existing laboratory workflows and information systems. Customers that have placed orders for our products include research institutions and commercial companies that plan to use the PacBio RS for clinical, basic and agricultural research, drug discovery and development, biosecurity and bio-fuels. Our customers are also interested in a number of other potential applications, including molecular diagnostics, food safety and forensics, which may require us to enhance the capabilities of our current products or develop additional products. To date, we have neither commercially launched nor generated any revenue from our products.

We believe that our SMRT technology has the potential to impact scientific study beyond DNA sequencing. We, and our scientific collaborators, have published a number of peer-reviewed articles in journals including *Science*, *Nature* and *Nature Methods* highlighting the power and potential applications of the SMRT platform. Potential applications that have been demonstrated include the study of chemical and structural modifications of DNA and the processing of ribonucleic acid, or RNA, and proteins, although these applications will not be available at commercial launch of the PacBio RS. We plan to provide these additional capabilities through enhancements to software and consumables without modifications to the PacBio RS hardware.

Evolution of Sequencing

Recent advances in the 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. The International Human Genome Project, designed to map the human genome, took 13 years at a cost of over \$3 billion and resulted in only approximately 92% coverage of the genome at its conclusion in 2004. The project generated many important insights regarding human biology, including a reduction in the number of estimated genes in the human genome from 100,000 or more to approximately 23,000. Despite these advances, researchers have not been able to fully characterize the human genome due to inherent limitations in existing technologies.

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First generation DNA sequencing, also called Sanger sequencing, was introduced in 1977 and has gradually grown into a \$600 million market. Under standard conditions, this method results in average readlength, defined as the number of individual bases identified contiguously, of approximately 700 bases, 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. The limited throughput of first generation sequencing technologies constrains the ability of researchers to sequence the large amounts of genetic material needed to unravel the complexities of many biological processes.

Second generation sequencing emerged in 2005 to address the issue of limited throughput. Since introduction, the market for these sequencing tools has grown rapidly and is currently estimated to be \$600 million. Second generation technologies rely on polymerase chain reaction, or PCR, amplification to generate numerous copies of a DNA sample to provide sufficient signal for detection. This amplification process can introduce errors in the DNA sequence known as amplification bias. In addition to introducing errors in the sequence, the process of amplification increases the complexity and time associated with sample preparation. Second generation tools are also characterized by a flush and scan sequencing process that, for many commercial second generation systems, results in long run times and decreased readlengths. The flush and scan sequencing process involves sequentially flushing in reagents, such as labeled nucleotides, incorporating the labeled nucleotides into the DNA strands, stopping the incorporation reaction, washing out the excess reagent, scanning to identify the incorporated base by virtue of the incorporated label and finally treating that base so that the strand is ready for the next flush and scan cycle. This repetitive process limits the average readlength produced by most second generation systems under standard sequencing conditions to approximately 35 to 400 bases. Long run times limit the flexibility of researchers to conduct experiments and short readlengths complicate the reassembly of sequences and the identification of disease-related variations in the genetic sequence.

Our Solution

We have developed a technology platform that enables single molecule, real-time, or SMRT, detection of biological processes. Based on our proprietary 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 and may also enable other types of biological research. The DNA sequencing market is expected to grow from \$1.2 billion in 2009 to more than \$3.6 billion by 2014 according to 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 genome centers, government and academic institutions, genomic service providers, pharmaceutical companies and agriculture companies.

Three key innovations underlie our SMRT technology platform:

The SMRT Cell. Our DNA sequencing is performed on proprietary SMRT Cells, each having an array of approximately 75,000 zero mode waveguides, or ZMWs. Each ZMW is a hole, tens of nanometers in diameter, which allows for limited penetration of focused laser light, creating a 30 nanometer observation window. Within this window, a DNA polymerase is immobilized on the surface of the ZMW and exposed to phospholinked nucleotides, allowing us to view labeled nucleotides being added into a growing DNA strand within the ZMW through the visualization of a fluorescent signal, or tag, associated with the nucleotide that is being added. The current 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 SMRT technology requires the use of our proprietary phospholinked nucleotides. These nucleotides have a fluorescent dye attached to the phosphate chain of the nucleotide rather than to the base, as is the case with other technologies. During the synthesis process, the phosphate chain is cleaved when the nucleotide is incorporated into the DNA strand. The DNA polymerase naturally frees the dye molecule from the nucleotide when it cleaves the phosphate chain

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leaving a completely natural piece of DNA with no evidence of labeling remaining. This removes the need for a flush and scan method as used in second generation sequencing, enabling long readlengths.

The PacBio RS. The PacBio RS is an instrument that conducts, monitors and analyzes single molecule biochemical reactions in real time. The instrument includes high performance optics, automated liquid handling, a touchscreen control interface, a computational Blade Center and software. The PacBio RS uses a high numerical aperture objective lens and four single-photon sensitive cameras to collect light emitted by fluorescent reagents allowing the observation of biological processes, such as the incorporation of labeled nucleotides during DNA synthesis. These observations are recorded as the biochemical events occur. An optimized set of algorithms is then used to translate this data into biologically relevant information, such as the composition of DNA strands known as base calls.

Our sequencing system includes the PacBio RS instrument and proprietary consumables, including SMRT Cells and reagent kits, providing a complete solution to the customer. A comprehensive informatics tools suite enabling users to generate finished sequence data is also included. The workflow begins with customers isolating their DNA samples of interest, which can come from a variety of sources, including humans, plants or animals, based on the nature of their scientific study. They then use our reagent kits to convert their DNA sample into a format that is compatible with our system. After loading their sample into the PacBio RS, they start the instrument run and real-time sequencing is performed. Our software is used for experimental design, instrument operation and interpretation of results.

We have instituted a limited production release program pursuant to which we have received orders for eleven limited production release instruments. Our limited production release customers include genome centers, clinical, government and academic institutions and an agricultural company. As of September 15, 2010, we have shipped a total of seven PacBio RS limited production release instruments, and we intend to ship the remaining four this year. Generally, each of these customers is obligated to pay us a deposit after accepting a limited production release instrument, and is entitled to receive an upgrade to a commercial release version of the PacBio RS, at which time each customer will be obligated to pay the balance of their order and we will then recognize revenue.

As of June 30, 2010, our backlog was approximately \$15 million, which includes both orders for limited production release instruments and full commercial release instruments received as of that date. We expect to deliver all orders in our backlog by December 31, 2011, however we do not expect to recognize revenue on any orders prior to December 31, 2010. The commercial launch of our first products is scheduled for early 2011. We cannot provide assurance that we will recognize revenue from these customers.

All of our revenue to date has been generated from government grants.

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 the sequencing reaction does not involve a time-consuming flush and scan process. In addition, our system does not require the routine PCR amplification needed by most second generation sequencing systems, thereby avoiding systematic amplification bias.

Longer readlengths. Our SMRT technology enables longer readlengths than most other commercially available sequencing methods largely due to the reagents and detection methods that we employ. Our technology uses a genetically modified DNA polymerase that maintains the natural processing activity of the polymerase while operating at a slower speed, enabling accurate detection of labeled nucleotides

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as they are added to a growing DNA strand. In nature, molecular events are intrinsically random, leaving uncertainty in the possible readlength of a particular sequencing reaction. Since our approach uses the natural processing activity of the polymerase, it produces a distribution of readlengths. We have demonstrated readlengths greater than 1,000 base pairs on average with instances of over 10,000 base pairs. We believe that the long readlengths produced by our SMRT technology will allow insights into biology that are not possible with existing technologies.

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. This speed enables the research community to ask and answer questions much faster than with 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.

Ease of use. We believe 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 and requires minimal user intervention.

Flexibility and granularity. The PacBio *RS* system enables 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. We call this granularity, and it results from our flexible consumables format. The ability to run a single SMRT Cell, or batch multiple SMRT Cells in a single run, provides flexibility in experiment design and implementation.

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 presence or absence of a methyl group can determine whether or not a gene is expressed in a particular cell, tissue or organism. The impact of such chemical modification of DNA on the expression of genes has been hypothesized to play a role in many diseases, including cancer. Importantly, it has been shown that changes in kinetics which can be detected automatically by the PacBio *RS*, may reflect the presence of DNA methylation.

Our Strategy

We plan to execute the following strategy:

Define the future of biological analysis based on SMRT technology. Our SMRT technology provides a window into biological processes that has not previously been available. We have and will continue to communicate the benefits and advantages of our SMRT technology platform through our commercial and marketing activities. In addition, we will continue to pursue publication of biological insights using our SMRT technology in top-tier scientific, peer-reviewed journals. We plan to continue to develop the applications of our SMRT technology in the field of DNA and to develop new applications in the fields of RNA and protein biology.

Focus initially on the DNA sequencing market. We will initially sell our products into the rapidly growing DNA sequencing market, addressing many of the limitations in current sequencing technologies and enabling a wide range of experiments and applications. We believe that the introduction of the PacBio *RS* will expand the market for genetic analysis tools. Customers that have placed orders for our products include research institutions and commercial companies that plan to use the PacBio *RS* for clinical, basic and agricultural research, drug discovery and development,

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biosecurity and bio-fuels. Our customers are also interested in a number of other potential applications, including molecular diagnostics, food safety and forensics, which may require us to enhance the capabilities of our current products or develop additional products.

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. These performance enhancements will be delivered through software upgrades and new consumables. 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 monitoring, RNA sequencing, protein translation and ligand binding, which is the biochemical interaction of a molecule with a second molecule or set of molecules. 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.

Risks Affecting Us

Our business is subject to a number of risks and uncertainties that you should understand before making an investment decision. These risks may have a material adverse effect on our business or operating results. These risks are discussed more fully in the section entitled "Risk Factors" following this prospectus summary. These include:

we are a development stage company with limited operating history and we have not recognized revenue from the sale of any products to date, including sales of our PacBio RS;

we have a cumulative loss from operations of \$246 million as of June 30, 2010, and we expect to continue to incur significant losses as we develop our business and may never achieve profitability;

we cannot be sure that the PacBio RS or any other products we expect to introduce will gain acceptance in the marketplace;

the PacBio RS and related consumable products we expect to introduce are highly complex, with unknown support requirements;

the PacBio RS may not meet the specifications required for full commercial release and we may not be able to produce other products with the specifications required by our customers;

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

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we may never earn revenue from our orders in backlog;

we have limited experience in selling and marketing our products and, as a result, may be unable to successfully commercialize our SMRT technology;

rapidly changing technology in life sciences could make the products we are developing obsolete and we may not be able to develop and manufacture new and improved products;

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we have limited experience in manufacturing our products, and we may be unable to establish manufacturing capacity for the PacBio RS or our consumable products in a timely manner or manufacture these products at a reasonable cost;

we may be unable to successfully scale the manufacturing process necessary to build and test multiple products on a full commercial basis; and

we may be unable to secure or maintain protection for our intellectual property and we are subject to litigation claiming that we infringe the intellectual property rights of others.

Corporate History and Information

We 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. Our website address is www.pacificbiosciences.com. Information contained on our website is not incorporated by reference into this prospectus, and should not be considered to be part of this prospectus.

In this prospectus, we, us and our refer to Pacific Biosciences of California, Inc. and its subsidiaries.

The names Pacific Biosciences, PacBio, SMRT, SMRTbell and our logo are our trademarks. All other trademarks and trade names appearing in this prospectus are the property of their respective owners.

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THE OFFERING

Common stock offered by us	Shares
Over-allotment option	Shares
Common stock to be outstanding after this offering	Shares

Use of proceeds

We intend to use the net proceeds from this offering to fund ongoing research and development of our products and SMRT technology, increases in our sales and marketing efforts associated with our planned commercial launch, increases in the scale of our manufacturing operations associated with producing our products and general corporate purposes, including working capital. We also may use a portion of the net proceeds to acquire complementary products, services, technologies or businesses. However, we have no understandings, agreements or commitments with respect to any such acquisition at this time. See Use of Proceeds.

Proposed NASDAQ Global Market symbol PACB

The number of shares of our common stock that will be outstanding following this offering is based on 75,227,061 shares of our common stock outstanding as of June 30, 2010 and excludes:

17,575,343 shares of common stock issuable upon the exercise of options outstanding as of June 30, 2010, with a weighted-average exercise price of \$2.70 per share;

50,569 shares of common stock issuable upon the exercise of warrants to purchase 50,569 shares of convertible preferred stock at a weighted-average exercise price of \$1.58 per share that upon the closing of this offering will represent warrants to purchase shares of common stock at a weighted-average exercise price of \$1.58 per share; and

11,537,206 shares of our common stock reserved for future issuance under our stock-based compensation plans, including 5,000,000 shares of common stock reserved for issuance under our 2010 Equity Incentive Plan, 1,500,000 shares of our common stock reserved for issuance under our 2010 Employee Stock Purchase Plan, 1,000,000 shares of our common stock reserved for issuance under our 2010 Outside Director Equity Incentive Plan, and shares that become available under the 2010 Equity Incentive Plan, 2010 Employee Stock Purchase Plan and 2010 Outside Director Equity Incentive Plan pursuant to provisions thereof that automatically increase the shares reserved for issuance under such plans, as more fully described in Executive Compensation Employee Benefit Plans. The 2010 Equity Incentive Plan, 2010 Employee Stock Purchase Plan and 2010 Outside Direct Equity Incentive Plan will become effective in connection with this offering.

Unless otherwise noted, the information in this prospectus reflects and assumes the following:

the conversion of all outstanding shares of our convertible preferred stock into an aggregate 73,305,523 of shares of common stock upon the closing of this offering;

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the conversion of all outstanding warrants to purchase shares of our convertible preferred stock into warrants to purchase 50,569 shares of common stock upon the closing of this offering;

no exercise after June 30, 2010 of options or warrants outstanding;

the effectiveness of our amended and restated certificate of incorporation upon the closing of this offering; and

no exercise by the underwriters of their over-allotment option.

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The summary statement of operations data below for the years ended December 31, 2007, 2008 and 2009 has been derived from our audited financial statements included elsewhere in this prospectus. The summary statement of operations data for the six-month periods ended June 30, 2009 and 2010 and the balance sheet data as of June 30, 2010 have been derived from our unaudited interim financial statements included elsewhere in this prospectus. Our historical results are not necessarily indicative of the results that may be expected in the future. The following summary financial data should be read in conjunction with Management's Discussion and Analysis of Financial Condition and Results of Operations and our financial statements and related notes included elsewhere in this prospectus.

	Years ended December 31,			Six-month periods ended	
	2007	2008	2009	2009	2010
	(in thousands, except share and per share amounts)				
Statements of operations data:					
Revenue	\$ 2,163	\$ 901	\$ 135	\$	\$ 1,174
Operating expenses					
Research and development	19,216	37,997	75,879	30,090	52,406
Sales, general and administrative	6,338	7,713	12,326	5,338	11,717
Total operating expenses	25,554	45,710	88,205	35,428	64,123
Loss from operations	(23,391)	(44,809)	(88,070)	(35,428)	(62,949)
Interest income (expense), net	1,940	1,157	451	327	(35)
Other income (expense), net	(67)	(102)	(84)	(10)	(55)
Net loss	\$ (21,518)	\$ (43,754)	\$ (87,703)	\$ (35,111)	\$ (63,039)
Basic and diluted net loss per share ⁽¹⁾	\$ (122.02)	\$ (62.02)	\$ (86.94)	\$ (37.76)	\$ (53.97)
Weighted-average shares outstanding used to calculate basic and diluted net loss per share ⁽¹⁾	176,342	705,451	1,008,781	929,856	1,168,063
Pro forma basic and diluted net loss per share (unaudited) ⁽¹⁾					
Pro forma weighted-average shares outstanding used to calculate basic and diluted net loss per share (unaudited) ⁽¹⁾					

- (1) Please see the notes to our financial statements appearing elsewhere in this prospectus for an explanation of the method used to calculate basic and diluted net loss per common share, the pro forma basic and diluted net loss per common share and the number of shares used in the computation of the per share amounts.

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The following table presents balance sheet data as of June 30, 2010 on an actual basis and on an as adjusted basis to reflect our sale of shares of common stock in this offering at an assumed initial public offering price of \$ _____ per share, the midpoint of the price range set forth on the front cover of this prospectus, after deducting estimated underwriting discounts and commissions and estimated offering expenses.

	As of June 30, 2010		Pro forma as adjusted ⁽²⁾⁽³⁾
	Actual	Pro forma ⁽¹⁾ (unaudited) (in thousands)	
Balance sheet data:			
Cash, cash equivalents and investments	\$ 138,756	\$ 138,756	\$
Working capital	123,896	123,896	
Total assets	152,897	152,897	
Convertible preferred stock warrant liability	282		
Convertible preferred stock	367,036		
Total stockholders' equity (deficit)	(235,650)	131,668	

- (1) The pro forma balance sheet data in the table above reflects (i) the conversion of all outstanding shares of convertible preferred stock into common stock and (ii) the reclassification of the convertible preferred stock warrant liability to additional paid-in capital, each effective upon the closing of this offering.
- (2) The pro forma as adjusted balance sheet data in the table above also reflects the pro forma conversions and reclassifications described immediately above plus the sale of _____ shares of our common stock in this offering at an assumed initial public offering price of \$ _____ per share, the midpoint of the range set forth on the cover page of this prospectus, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.
- (3) A \$1.00 increase (decrease) in the assumed initial public offering price of \$ _____ per share, the midpoint of the range set forth on the cover page of this prospectus, would increase (decrease) cash, cash equivalents and investments, and working capital, total assets and total stockholders' equity (deficit) by \$ _____ million, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same, and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. Each increase of 1.0 million shares in the number of shares offered by us would increase cash, cash equivalents, investments, and working capital, total assets and total stockholders' equity (deficit) by approximately \$ _____ million. Similarly, each decrease of 1.0 million shares in the number of shares offered by us would decrease cash, cash equivalents and investments, and each of working capital, total assets and total stockholders' equity (deficit) by approximately \$ _____ million. The pro forma as adjusted information discussed above is only illustrative and will be adjusted based on the actual public offering price and other terms of this offering determined at pricing.

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RISK FACTORS

Investing in our common stock involves a high degree of risk. You should consider carefully the risks and uncertainties described below, together with all of the other information in this prospectus, including our financial statements and related notes, before deciding whether to purchase shares of our common stock. If any of the following risks is realized, our business, financial condition, results of operations and prospects could be materially and adversely affected. In that event, the price of our common stock could decline, and you could lose part or all of your investment.

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 we may base our projected revenue. We have limited historical financial data upon which we may base our planned operating expense or upon which you may 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;

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. You should consider the risks and difficulties frequently encountered by companies like ours in new and rapidly evolving markets when making a decision to invest in our common stock.

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 generated no 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. As of June 30, 2010, we had an accumulated deficit of \$255.0 million. 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, or to 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 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, which applications are more fully described under the subheading **Future Commercial Applications** on page 64. 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.

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

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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.

We may never earn revenue from our orders in backlog.

As of June 30, 2010 we had orders in backlog totaling approximately \$15.0 million. This figure 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 the products we are developing, 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 that develop as a result of technological and scientific advances. These new market opportunities may be outside the scope of our proven expertise or in areas which have unproven market demand, and the utility and value of new products and services developed by us may not be accepted in the markets served by the new products. 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 these 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 we introduce 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.

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

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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.

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 being able to attract customers for our products. Although members of our sales and marketing team have considerable industry experience and have engaged in marketing activities for our products, in the future we must expand our sales, marketing, distribution and customer support capabilities with the appropriate technical expertise 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 force 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 one or more 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 establish manufacturing capacity by ourselves or with partners in a timely manner, commercialization of our products would be delayed, which would result in lost revenue and harm our business.

In order to commercialize our products in volume, we need to either build additional internal manufacturing capacity or contract with one or more 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 unexpected difficulties in manufacturing our products. There is no assurance that we will be able to continue to build manufacturing capacity internally or find one or more suitable manufacturing partners, or both, 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 and cameras. If we were required to purchase these components from an alternative source, it could take several months or longer to

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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.

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

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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.

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 has been experiencing a significant economic downturn, and global credit and capital markets have experienced substantial 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 your investments. 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

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resources to invest in new technologies, more substantial experience in new product development and manufacturing capabilities and more established distribution channels to deliver products to customers than we do. These competitors may be able to respond more quickly and effectively than we can to new or changing opportunities, technologies, standards or customer requirements. In light of these advantages, even if our technology is more effective than the products or service offerings of our competitors, current or potential customers might accept competitive products and services in lieu of purchasing our technology. Increased competition is likely to 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 assure you that a material performance problem 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 written notice of 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.

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 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

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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. Until recently we have limited our accounting and internal control structure to meet the external financial reporting obligations required by the terms of the private equity purchased and held by our investors. The rapid growth of our operations and the planned initial public offering created a need for additional resources within the accounting and finance functions due to the increasing need to produce timely financial information and to ensure the level of segregation of duties customary for a U.S. public company. We have since hired additional resources in the accounting and finance function and continue to reassess the sufficiency of finance personnel in response to these increasing demands and expectations.

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 expect that 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 controls 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 will incur additional accounting, legal and other expenses that we did not incur as a private company. We will incur costs associated with our public company reporting requirements. We also anticipate that we will incur costs associated with corporate governance requirements, including requirements under the Sarbanes-Oxley Act of 2002, 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 limits and coverage or incur substantially higher costs to obtain the same or similar coverage. The impact of these requirements could also

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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.

As of December 31, 2009, our available net operating losses totaled \$151.9 million. In general, 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. In addition, if we undergo an ownership change in connection with or after this public offering, our ability to utilize our NOLs could be further limited by Section 382. Future changes in our stock ownership, some of which are outside of our control, could result in additional ownership changes under Section 382. We are unable to predict the future ownership and other variables considered by, and elections available pursuant to, Section 382 for concluding on the usability of our net operating losses. Should an ownership change pursuant to Section 382 result from this offering, we do not believe it will result in a limitation of the usability of our net operating losses. We may not be able to utilize a material portion of our NOLs, even if we attain profitability.

Risks Related to Our Intellectual Property

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

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

we or our licensors might not have been the first to make the inventions covered by each of our pending patent applications or issued patents;

we or our licensors might not have been the first to file patent applications for these inventions;

it is possible that neither our pending patent applications nor the pending patent applications of our licensors will result in issued patents;

our patents or the patents of our licensors may not be of sufficient scope to prevent others from practicing our technologies, developing competing products, designing around our patented technologies or independently developing similar or alternative technologies;

our and our licensors' patent applications or patents have been, and may in the future be, subject to interference, opposition or similar administrative proceedings, which could result in those patent applications failing to issue as patents, those patents being held invalid or the scope of those patents being substantially reduced;

we may not adequately protect our trade secrets;

we may not develop additional proprietary technologies that are patentable; or

the patents of others may limit our freedom to operate and prevent us from commercializing our technology in accordance with our plans.

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

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

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

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

We license from third parties some of the intellectual property that is important to our business, 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 Business - Intellectual Property, 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, 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. For example, we are presently involved in a patent interference with Life Technologies Corporation, or Life, related to U.S. Patent No. 7,329,492, that was acquired by Life in its acquisition of Visigen Biotechnologies, Inc., and U.S. Patent Application Serial No. 11/459,182, owned by us, in which the parties are each claiming entitlement to patent claims directed to a type of single molecule, real-time sequencing technology. For more information on this proceeding, please see [Business Legal Proceedings](#) below. 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

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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 Business 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 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,

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which could include permitting the use of such software and source code at no cost to the user. Open source license terms are often ambiguous, and there is little legal precedent governing the interpretation of these licenses. Successful claims made by the licensors of open source software that we have violated the terms of these licenses could result in unanticipated obligations including being subject to significant damages, being enjoined from distributing products that incorporate open source software, and being required to make available our proprietary source code pursuant to an open source license, which could substantially help our competitors develop products that are similar to or better than ours and otherwise adversely affect our business.

Risks Relating to Owning Our Common Stock and This Offering

Our share price may be volatile, and you may be unable to sell your shares at or above the offering price.

The initial public offering price for our shares was determined by negotiations between us and representatives of the underwriters and may not be indicative of prices that will prevail in the trading market. 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 our executive officers, directors and stockholders; and

general economic and market conditions.

Furthermore, the stock markets have experienced extreme 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 after this offering does not exceed the initial public offering price, you may not realize any return on your investment in us and may lose some or all of your investment. In the past,

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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.

No public market for our common stock currently exists, and an active trading market may not develop or be sustained following this offering.

Prior to this offering, there has been no public market for our common stock. An active trading market may not develop following the closing of this offering or, if developed, may not be sustained. The lack of an active market may impair your ability to sell your shares at the time you wish to sell them or at a price that you consider reasonable. The lack of an active market may also reduce the fair market value of your shares. An inactive market may also impair our ability to raise capital to continue to fund operations by selling shares and may impair our ability to acquire other companies or technologies by using our shares as consideration. The initial public offering price was determined by negotiations between us and the underwriters and may not be indicative of the future prices of our common stock.

If securities or industry analysts do not publish research or reports about our business or publish negative reports about our business, our share price and trading volume could decline.

The trading market for our common stock will depend on the research and reports that securities or industry analysts publish about us or our business. Currently, we do not have any analyst coverage and we may not obtain analyst coverage in the future. In the event we obtain analyst coverage, we will not have any control over such analysts. If one or more of the analysts who cover us downgrade our 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 in the public market could cause our share price to fall.

Sales of a substantial number of shares of our common stock in the public market after this offering, or the perception that these sales might occur, could depress the market price of our common stock and could impair our ability to raise capital through the sale of additional equity securities. Based on the number of shares of common stock outstanding as of June 30, 2010, upon the closing of this offering, we will have _____ shares of common stock outstanding, assuming no exercise of our outstanding options.

All of the common stock sold in this offering will be freely tradable without restrictions or further registration under the Securities Act of 1933, as amended, referred to as the Securities Act, except for any shares held by our affiliates as defined in Rule 144 under the Securities Act. The remaining 75,227,061 common stock outstanding after this offering, based on shares outstanding as of June 30, 2010, will be restricted as a result of securities laws, lock-up agreements or other contractual restrictions that restrict transfers for at least 180 days after the date of this prospectus, subject to certain extensions.

The underwriters may, in their sole discretion, release all or some portion of the shares subject to lock-up agreements with the underwriters prior to expiration of the lock-up period. See [Shares Eligible for Future Sale](#) below.

The holders of 67,080,613 common stock, or 89.2% based on shares outstanding as of June 30, 2010, and holders of warrants to purchase 50,569 shares of 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. See [Certain Relationships and Related Party Transactions](#) [Investor Rights Agreement](#) below. 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

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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 intend to file a registration statement on Form S-8 under the Securities Act to register 33,671,239 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.

Our management team may invest or spend the proceeds of this offering in ways with which you may not agree or in ways which may not yield a return.

We intend to use the net proceeds from this offering to fund ongoing research and development of our products and SMRT technology, increases in our sales and marketing efforts associated with our planned commercial launch, increases in the scale of our manufacturing operations associated with producing our products and general corporate purposes, including working capital as outlined in Use of Proceeds elsewhere in this prospectus. Although we may also use a portion of the net proceeds to acquire complementary products, services, technologies or businesses, we have no current understandings, agreements or commitments to do so at this time.

Our management will have considerable discretion in the application of the net proceeds, and you will not have the opportunity, as part of your investment decision, to assess whether the proceeds are being used appropriately. The net proceeds may be used for corporate purposes that do not increase our operating results or market value. Until the net proceeds are used, they may be placed in investments that do not produce significant income or that may lose value.

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

Upon completion of this offering, our existing significant stockholders, executive officers, directors and their affiliates will beneficially own, in the aggregate, approximately % of our outstanding shares of common stock, and if the underwriters' option to purchase additional shares is exercised in full, such persons and their affiliates will beneficially own, in the aggregate, approximately % 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 upon the closing of this offering, 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, which will become effective upon the closing of this offering, 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 shares of authorized but unissued shares of common stock;

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

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

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

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

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

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

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

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

After the completion of this offering, we expect to have approximately _____ shares of authorized but unissued shares of common stock. Our board of directors may issue shares of common stock from this authorized but unissued pool from time to time without stockholder approval, resulting in the dilution of our existing stockholders.

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

We have never declared or paid any cash dividends on our common stock and do not intend to pay any cash dividends in the foreseeable future. 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.

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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS AND INDUSTRY DATA

This prospectus contains forward-looking statements that are based on our management's beliefs and assumptions and on information currently available to our management. The forward-looking statements are contained principally in Prospectus Summary, Risk Factors, Management's Discussion and Analysis of Financial Condition and Results of Operations, Business and Compensation Discussion and Analysis. Forward-looking statements include information concerning our possible or assumed future results of operations, business strategies, financing plans, competitive position, industry environment, potential growth opportunities and the effects of competition. Forward-looking statements include all statements that are not historical facts and can be identified by terms such as anticipates, believes, could, seeks, estimates, expects, intends, may, plans, potential, predicts, projects, should, will, would or similar expressions and the negatives of those terms.

Forward-looking statements involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. We discuss these risks in greater detail in Risk Factors and elsewhere in this prospectus. Given these 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 prospectus. You should read this prospectus and the documents that we have filed as exhibits to the registration statement, of which this prospectus is a part, completely and with the understanding that our actual future results may be materially different from what we expect.

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.

This prospectus also contains estimates and other information concerning our industry, including market size and growth rates, that are based on industry publications, surveys and forecasts, including those generated by Scientia Advisors. This information involves a number of assumptions and limitations, and you are cautioned not to give undue weight to these estimates. These industry publications, surveys and forecasts generally indicate that their information has been obtained from sources believed to be reliable. The industry in which we operate is subject to a high degree of uncertainty and risk due to variety of factors, including those described in Risk Factors.

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USE OF PROCEEDS

We estimate that the net proceeds from our sale of _____ shares of common stock in this offering at an assumed initial public offering price of \$ _____ per share, the midpoint of the price range set forth on the front cover of this prospectus, after deducting estimated underwriting discounts and commissions and estimated offering expenses, will be approximately \$ _____ million, or \$ _____ million if the underwriters option to purchase additional shares is exercised in full. A \$1.00 increase (decrease) in the assumed initial public offering price would increase (decrease) the net proceeds to us from this offering by \$ _____ million, assuming the number of shares offered by us, as set forth on the front cover of this prospectus, remains the same and after deducting the estimated underwriting discounts and commissions.

Although our plans will be subject to revision, assuming an estimated aggregate offering of \$200 million resulting in net proceeds to us of approximately \$180 million, we plan to invest \$60 million to \$70 million in current and future applications of our SMRT technologies, use \$40 million to \$60 million to fund our anticipated future working capital needs, \$20 million to \$30 million to fund planned capital expenditures and \$40 million to \$60 million for other general corporate purposes, including, but not limited to, operating expenses, business development activities and operating as a public company. In the event that the underwriters option to purchase additional shares is exercised, the proceeds will be used to fund our anticipated future working capital needs.

We also may use a portion of the net proceeds to acquire complementary products, services, technologies or businesses. However, we have no understandings, agreements or commitments with respect to any such acquisition at this time.

Pending their use, we plan to invest our net proceeds from this offering in short-term, interest-bearing obligations, investment-grade instruments, certificates of deposit or direct or guaranteed obligations of the U.S. government.

DIVIDEND POLICY

We have never declared or paid cash dividends on our common stock. We currently intend to retain all available funds and any future earnings for use in the operation of our business and do not anticipate paying any dividends on our common stock in the foreseeable future. Any future determination to declare dividends will be made at the discretion of our board of directors and will depend on our financial condition, operating results, capital requirements, general business conditions and other factors that our board of directors may deem relevant.

Table of Contents**CAPITALIZATION**

The following table sets forth our capitalization as of June 30, 2010 on:

an actual basis;

on a pro forma basis to reflect the conversion of all outstanding shares of our convertible preferred stock into 73,305,523 shares of our common stock upon the closing of this offering, the reclassification of our outstanding warrants to purchase convertible preferred stock into warrants to purchase 50,569 shares of common stock upon the closing of this offering and the effectiveness of our amended and restated certificate of incorporation upon the closing of this offering; and

on a pro forma as adjusted basis to reflect the pro forma adjustments described above and our receipt of the net proceeds from our sale of _____ shares of common stock in this offering at an assumed initial public offering price of \$ _____ per share, the midpoint of the price range set forth on the front cover of this prospectus, after deducting estimated underwriting discounts and commissions and estimated offering expenses.

The information below is illustrative only and our capitalization following the closing of this offering will be adjusted based on the actual initial public offering price and other terms of this offering determined at pricing. You should read this table together with Management's Discussion and Analysis of Financial Condition and Results of Operations and our financial statements and the related notes appearing elsewhere in this prospectus.

	June 30, 2010		Pro forma as adjusted⁽¹⁾
	Actual	Pro forma (in thousands)	
Facility financing obligation, less current portion	\$ 2,955	\$ 2,955	\$
Convertible preferred stock warrant liability	282		
Convertible preferred stock, \$0.0001 par value; 153,394,052 shares authorized, 73,305,523 shares issued and outstanding, actual; no shares authorized, none issued or outstanding, pro forma and pro forma as adjusted	367,036		
Stockholders' equity (deficit):			
Preferred stock, \$0.0001 par value; no shares authorized, issued or outstanding, actual; 50,000,000 shares authorized, no shares issued or outstanding, pro forma and pro forma as adjusted			
Common stock, \$0.0001 par value; 121,668,835 shares authorized, 1,921,538 shares issued and outstanding, actual; 1,000,000,000 shares authorized, 75,227,061 shares issued and outstanding, pro forma; and 1,000,000,000 shares authorized, _____ shares issued and outstanding, pro forma as adjusted		8	
Additional paid-in capital ⁽¹⁾	19,395	386,705	
Accumulated other comprehensive income (loss)	(5)	(5)	
Accumulated deficit	(255,040)	(255,040)	
Total stockholders' equity (deficit) ⁽⁴⁾	(235,650)	131,668	
Total capitalization ⁽¹⁾	\$ 134,623	\$ 134,623	\$

(1)

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A \$1.00 increase (decrease) in the assumed initial public offering price of \$ _____ per share, the midpoint of the range set forth on the cover page of this prospectus, would increase (decrease) each of additional paid-in capital, total stockholders' equity and total capitalization by \$ _____ million, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same, and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. Each increase of 1.0 million shares in the number of shares offered by us, together with a \$1.00 increase

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in the assumed offering price of \$ per share, would increase additional paid-in capital, total stockholders' equity and total capitalization by approximately \$ million.

The number of shares of our common stock that will be outstanding following this offering is based on 75,227,061 shares of our common stock outstanding as of June 30, 2010 and excludes:

17,575,343 shares of common stock issuable upon the exercise of options outstanding as of June 30, 2010, with a weighted-average exercise price of \$2.70 per share;

50,569 shares of common stock issuable upon the exercise of warrants to purchase 50,569 shares of convertible preferred stock at a weighted-average exercise price of \$1.58 per share that upon the closing of this offering will represent warrants to purchase shares of common stock at a weighted-average exercise price of \$1.58 per share; and

11,537,206 shares of our common stock reserved for future issuance under our stock-based compensation plans, including 5,000,000 shares of common stock reserved for issuance under our 2010 Equity Incentive Plan, 1,500,000 shares of our common stock reserved for issuance under our 2010 Employee Stock Purchase Plan, 1,000,000 shares of our common stock reserved for issuance under our 2010 Outside Director Equity Incentive Plan, and shares that become available under the 2010 Equity Incentive Plan, 2010 Employee Stock Purchase Plan and 2010 Outside Director Equity Incentive Plan pursuant to provisions thereof that automatically increase the shares reserved for issuance under such plans, as more fully described in Executive Compensation Employee Benefit Plans. The 2010 Equity Incentive Plan, 2010 Employee Stock Purchase Plan and 2010 Outside Director Equity Incentive Plan will become effective in connection with this offering.

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If you invest in our common stock, your interest will be diluted to the extent of the difference between the amount per share paid by purchasers of shares of common stock in this initial public offering and the pro forma as adjusted net tangible book value per share of common stock immediately after the closing of this offering.

At June 30, 2010, our net tangible book value was approximately \$(235.7) million, or \$(122.64) per share of common stock. Net tangible book value per share represents the amount of our total tangible assets less our total liabilities, divided by the shares of common stock outstanding at June 30, 2010. At June 30, 2010 our pro forma net tangible book value was \$131.7 million, or \$1.75 per share of common stock. Our pro forma net tangible book value per share represents the amount of our tangible total assets less our total liabilities divided by the total number of shares of our common stock outstanding at June 30, 2010, after giving effect to the conversion of our preferred stock into common stock upon the closing of this offering and the reclassification of our preferred stock warrant liability to additional paid in capital upon the conversion of warrants to purchase shares of our convertible preferred stock into warrants to purchase shares of our common stock upon the closing of this offering.

After giving effect to our sale of _____ shares of common stock in this offering at an assumed initial public offering price of \$ _____, the midpoint of the price range set forth on the front cover of this prospectus, and after deducting estimated underwriting discounts and commissions and estimated offering expenses, our pro forma as adjusted net tangible book value at June 30, 2010 would have been \$ _____, or \$ _____ per share of common stock. This represents an immediate increase in pro forma as adjusted net tangible book value of \$ _____ per share to existing stockholders and an immediate dilution of \$ _____ per share to new investors.

The following table illustrates this dilution.

Assumed initial public offering price per share	\$
Pro forma net tangible book value per share as of June 30, 2010	\$
Increase per share attributable to this offering	
Pro forma as adjusted net tangible book value per share after this offering	
Pro forma net tangible book value dilution per share to new investors in this offering	\$

If all our outstanding options had been exercised, the pro forma net tangible book value as of June 30, 2010 would have been \$179.2 million, or \$1.93 per share, and the pro forma net tangible book value after this offering would have been \$ _____ million, or \$ _____ per share, causing dilution to new investors of \$ _____ per share.

If the underwriters exercise their option to purchase additional shares in full, the pro forma as adjusted net tangible book value will increase to \$ _____ per share, representing an immediate increase to existing stockholders of \$ _____ per share and an immediate dilution of \$ _____ per share to new investors.

The following table summarizes, on a pro forma as adjusted basis as of June 30, 2010, the total number of shares of common stock purchased from us, the total consideration paid to us, and the average price per share paid to us by existing stockholders and by new investors purchasing shares in this offering at the initial public offering price of \$ _____, the midpoint of the price range set forth on the front cover of this prospectus, before deducting estimated underwriting discounts and commissions and estimated offering expenses.

	Shares purchased		Total consideration		Average price Per share
	Number	Percent	Amount	Percent	
Existing stockholders		%	\$	%	\$
New investors					
Total		%	\$	%	

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If the underwriters exercise their option to purchase additional shares in full, our existing stockholders would own % and our new public investors would own % of the total number of shares of our common stock outstanding upon the closing of this offering.

The foregoing calculations are based on 75,227,061 shares of our common stock outstanding as of June 30, 2010 and exclude:

17,575,343 shares of common stock issuable upon the exercise of options outstanding as of June 30, 2010, with a weighted-average exercise price of \$2.70 per share;

50,569 shares of common stock issuable upon the exercise of warrants to purchase 50,569 shares of convertible preferred stock at a weighted-average exercise price of \$1.58 per share that upon the closing of this offering will represent warrants to purchase shares of common stock at a weighted-average exercise price of \$1.58 per share; and

11,537,206 shares of our common stock reserved for future issuance under our stock-based compensation plans, including 5,000,000 shares of common stock reserved for issuance under our 2010 Equity Incentive Plan, 1,500,000 shares of our common stock reserved for issuance under our 2010 Employee Stock Purchase Plan, 1,000,000 shares of our common stock reserved for issuance under our 2010 Outside Director Equity Incentive Plan, and shares that become available under the 2010 Equity Incentive Plan, 2010 Employee Stock Purchase Plan and 2010 Outside Director Equity Incentive Plan pursuant to provisions thereof that automatically increase the shares reserved for issuance under such plans; as more fully described in Executive Compensation Employee Benefit Plans. The 2010 Equity Incentive Plan, 2010 Employee Stock Purchase Plan and 2010 Outside Director Equity Incentive Plan will become effective in connection with this offering.

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This selected statement of operations data for the years ended December 31, 2007, 2008 and 2009 and selected balance sheet data as of December 31, 2008 and 2009 have been derived from our audited financial statements and related notes included elsewhere in this prospectus. The summary statement of operations data for the six-month periods ended June 30, 2009 and 2010 and the balance sheet data as of June 30, 2010 have been derived from our unaudited financial statements included elsewhere in this prospectus. The statement of operations data for the years ended December 31, 2005 and 2006 and the balance sheet data as of December 31, 2005, 2006 and 2007 has been derived from our audited financial statements not included in this prospectus. The unaudited interim financial statements have been prepared on the same basis as the annual financial statements and reflect all adjustments necessary to fairly state our financial position as of June 30, 2010 and results of operations for the six-month periods ended June 30, 2009 and 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 financial statements and related notes included elsewhere in this prospectus.

	2005	2006	Years ended December 31, 2007 2008		2009	Six-month periods ended June 30, 2009 2010	
			(in thousands, except share and per share amounts)				
Statement of Operations Data:							
Revenue	\$ 1,400	\$ 2,011	\$ 2,163	\$ 901	\$ 135	\$	\$ 1,174
Operating expenses							
Research and development ⁽¹⁾	8,688	10,364	19,216	37,997	75,879	30,090	52,406
Sales, general and administrative ⁽¹⁾	3,652	3,501	6,338	7,713	12,326	5,338	11,717
Total operating expenses	12,340	13,865	25,554	45,710	88,205	35,428	64,123
Loss from operations	(10,940)	(11,854)	(23,391)	(44,809)	(88,070)	(35,428)	(62,949)
Interest income (expense), net	82	271	1,940	1,157	451	327	(35)
Other income (expense), net	(19)	(105)	(67)	(102)	(84)	(10)	(55)
Net loss	\$ (10,877)	\$ (11,688)	\$ (21,518)	\$ (43,754)	\$ (87,703)	\$ (35,111)	\$ (63,039)
Basic and diluted net loss per share ⁽²⁾	(*)	(*)	\$ (136.46)	\$ (66.91)	\$ (86.52)	\$ (37.69)	\$ (49.79)
Weighted-average shares outstanding used to calculate basic and diluted net loss per share ⁽²⁾		1,993	157,683	653,910	1,013,730	931,511	1,266,038
Pro forma net loss per share basic and diluted (unaudited) ⁽²⁾					\$ (1.58)		\$ (1.01)
Pro forma weighted-average shares outstanding used to calculate net loss per share basic and diluted (unaudited) ⁽³⁾					55,477,488		62,405,225

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	2005	2006	As of December 31, 2007 2008		2009	June 30, 2010
			(in thousands)			
Balance Sheet Data:						
Cash, cash equivalents and investments	\$ 9,686	\$ 50,090	\$ 30,090	\$ 106,051	\$ 92,735	\$ 138,756
Working capital	8,349	48,043	27,082	102,224	85,326	123,896
Total assets	11,894	52,533	34,349	113,107	101,098	152,897
Notes payable ⁽³⁾	2,100	2,092	1,700	1,300		
Convertible preferred stock warrant liability		140	151	142	226	282
Convertible preferred stock	31,649	81,154	81,222	201,085	269,101	367,036
Total stockholders' deficit	(23,019)	(32,412)	(52,135)	(93,389)	(177,123)	(235,650)

- (1) Includes stock-based compensation expense. For further information, see "Stock Option Plans" in the Notes to Financial Statements of this prospectus.
- (2) For further information, see "Summary of Significant Accounting Policies - Net Loss Per Share and Pro Forma Net Loss Per Share" in the Notes to Financial Statements of this prospectus for an explanation of the method used to calculate basic and diluted net loss per share of common stock, the pro forma 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) For further information, see "Facility Financing and Debt Obligations" in the Notes to Financial Statements of this prospectus for an explanation of our notes payable.
- (*) Due to the limited number of weighted-average unrestricted shares of our common stock outstanding during 2005 and 2006 the calculated net loss per share is not meaningful.

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**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 financial statements and the related notes appearing at the end of this prospectus. Some of the information contained in this discussion and analysis or set forth elsewhere in this prospectus, 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 prospectus 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. Our revenue to date has come from U.S. government grants. Our operations to date have been primarily focused on developing our technology, undertaking engineering activities to develop our products and conducting initial marketing of our products. We operate in a single segment. From inception through June 30, 2010, we have received net proceeds of \$356.0 million from the issuance of convertible preferred stock. All of our outstanding convertible preferred stock will automatically convert into common stock upon the closing of this offering.

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 June 30, 2010, we had a deficit accumulated during the development stage of \$255.0 million. We incurred net losses of \$21.5 million, \$43.8 million and \$87.7 million in 2007, 2008 and 2009, 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 for 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. For the six-month period ended June 30, 2010 we have earned approximately \$1.2 million in funding from U.S. government grants.

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

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.

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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 the delivery of a full commercial release unit. 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, 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. In the near term, we expect to hire additional employees, as well as incur contract-related expense, as we continue to invest in the development of our products.

Since inception, we have incurred approximately \$206.7 million of research and development expense. In 2010, we incurred approximately \$3.6 million in prototype expense included in research and development that we do not expect to recur in 2011. In addition, manufacturing related expenses in 2010 were recorded in research and development expense as we have not yet recorded revenue. We expect that our research and development expense in 2011 will decline as compared to 2010 as we transition to commercial operations.

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 on investment balances. Our interest income will vary each reporting period depending on our average investment balances during the period and market interest rates. We expect interest income to fluctuate in the future with changes in average investment balances and market interest rates. Interest income (expense), net also includes interest expense relating to loan and debt agreements and facility financing obligations resulting from lease agreements. 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. Our outstanding convertible preferred stock warrants are classified as liabilities and, as such, are marked-to-market at each balance sheet date with the corresponding gain or loss from the adjustment recorded as other income (expense), net. We will continue to record adjustments to the fair value of the warrants until they are exercised, automatically converted into warrants to purchase common stock or expire, at which time the warrants will no longer be remeasured at each balance sheet date. Upon the closing of this offering, our outstanding warrants will automatically convert into warrants to purchase common stock.

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.

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Critical Accounting Policies and Estimates

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

Convertible Preferred Stock Warrants

We classify freestanding warrants to purchase shares of our convertible preferred stock as liabilities on our balance sheets at fair value because the warrants may conditionally obligate us to redeem the underlying convertible preferred stock at some point in the future. The warrants are subject to remeasurement at each balance sheet date, and any change in fair value is recognized as a component of other income (expense), net in the statements of operations. We estimate the fair value of these warrants at the respective balance sheet dates using the Black-Scholes option pricing model. We use a number of assumptions to estimate the fair value, including the remaining contractual terms of the warrant, risk-free interest rates, expected dividend yield and expected volatility of the price of the underlying common stock. These assumptions are highly judgmental and could differ significantly in the future.

During 2007, 2008 and 2009, we recorded charges (gains) of \$10,000, \$(9,000) and \$84,000, respectively, through other income (expense), net to reflect the change in the fair value of the warrants. For the six-month periods ended June 30, 2009 and 2010 we recorded charges of \$10,000 and \$56,000, respectively, as a result of an increase in the fair value of the warrants.

Valuation of Stock-based Awards, Common Stock and Warrants

Stock-based Compensation

Prior to January 1, 2006, we accounted for our stock options granted to employees using the intrinsic value method. The intrinsic value method requires the recognition of compensation expense for stock options granted to employees based on differences between the exercise price of the stock options granted and the fair value of the underlying common stock. Pursuant to the intrinsic value method, any compensation cost relating to stock options was recorded on the date of the grant as a component of stockholders' equity as deferred compensation and was subsequently amortized to expense over the vesting period of the award. We generally did not recognize stock-based compensation for stock options granted to our employees prior to January 1, 2006 as we granted stock options with an exercise price equal to the fair value of the underlying common stock.

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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.

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 each new employee option awarded 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,			Six-month periods ended	
	2007	2008	2009	2009	2010
				(unaudited)	
Expected term	7.0 years	7.0 years	5.7 years	5.7 years	5.9 years
Expected volatility	60%	50 - 52%	46 - 48%	48%	46 - 55%
Risk-free interest rate	3.5 - 5.1%	2.8 - 3.5%	1.8 - 3.0%	1.8 - 3.0%	2.2 - 2.6%
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 Black-Scholes option pricing model requires inputs such as the risk-free interest rate, expected term and expected volatility. Further, the forfeiture rate also affects the amount of aggregate compensation. These inputs are subjective in nature and generally require us to apply significant judgment.

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 life. 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.

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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. Quarterly changes in the estimated forfeiture rate can have a significant effect on reported stock-based compensation expense, as the cumulative effect of adjusting the rate for all expense amortization is recognized in the period the forfeiture estimate is changed. If a revised forfeiture rate is higher than the previously estimated forfeiture rate, an adjustment is made that will result in a decrease to the stock-based compensation expense recognized in the financial statements. If a revised forfeiture rate is lower than the previously estimated forfeiture rate, an adjustment is made that will result in an increase to the stock-based compensation expense recognized in the financial statements. The effects of forfeiture adjustments during the years ended December 31, 2007, 2008, 2009 and the six-month period ended June 30, 2010 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 lives 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.

We recognized stock-based compensation expense related to employees and non-employees as follows:

	Years ended December 31,			Six-month periods ended	
	2007	2008	2009	2009	2010
	(in thousands)				
Research and development	\$ 398	\$ 1,183	\$ 2,314	\$ 1,062	\$ 2,498
Sales, general and administrative	184	387	748	332	1,242
Total stock-based compensation expense	\$ 582	\$ 1,570	\$ 3,062	\$ 1,394	\$ 3,740

As of June 30, 2010, we had \$15.8 million of unrecognized stock-based compensation expense, net of estimated forfeitures, that is expected to be recognized over a weighted-average period of 3.3 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.

We also account for stock options issued to non-employees based on their estimated fair value determined using the Black-Scholes option pricing model. However, the fair value of the equity awards granted to non-employees is remeasured as the awards vest, and the resulting increase in value, if any, is recognized as expense during the period the related services are rendered.

Common Stock Valuation

The fair values of the common stock underlying stock options granted through 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. We believe that the composition of our board of directors resulted in a fair and reasonable view of the stock value and, together with the board of directors' cumulative knowledge of, and experience with, similar companies, resulted in a fair valuation of our common stock.

Given the absence of a public trading market, 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

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liquidity event, such as an initial public offering, or IPO, given prevailing market conditions. If we had made different assumptions and estimates, the amount of our stock-based compensation expense could have been materially different. We believe that we have used reasonable methodologies, approaches and assumptions in determining the fair value of our common stock.

Factors Considered and Methodologies Used in Determining Common Stock Fair Value

In valuing our common stock, we determine our business equity value by taking a weighted combination of the value indications using two valuation approaches, an income approach and a market approach.

The income approach estimates the present value of future estimated cash flows, based upon forecasted revenue and costs. These discounted cash flows are added to the present value of our estimated enterprise terminal value. These future cash flows are discounted to their present values using a discount rate corresponding to our estimated required rate of return. The discount rate is derived from an analysis of the cost of capital of our publicly traded peer group as of each valuation date and is adjusted to reflect the risks inherent in our cash flows.

The market approach estimates the fair value of a company by applying the market multiples of comparable publicly traded companies. We calculate a multiple of key metrics implied by the enterprise values or acquisition values of our publicly traded peers. Based on the range of these observed multiples, we apply judgment in determining an appropriate multiple to apply to our metrics in order to derive an indication of value.

Once we determine the fair value, we use two methods to allocate our company value to each of our classes of stock, the Option Pricing Method and the Probability Weighted Expected Return Method.

The Option Pricing Method values each equity class by creating a series of call options on our enterprise value, with exercise prices based on the liquidation preferences, participation rights and strike prices of derivatives. This method is generally preferred when future outcomes are difficult to predict and dissolution or liquidation is not imminent.

The Probability Weighted Expected Return Method involves a forward-looking analysis of the possible future outcomes of the enterprise. This method is particularly useful when discrete future outcomes can be predicted at a high confidence level with a probability distribution. Discrete future outcomes considered under the Probability Weighted Expected Return Method included non-IPO market based outcomes as well as IPO scenarios. In the non-IPO scenario, a large portion of our equity value is allocated to our convertible preferred stock as the aggregate liquidation preference was approximately \$258.8 million at December 31, 2009. In the IPO scenario, the equity value is allocated pro rata among the shares of common stock and each series of convertible preferred stock, which causes our common stock to have a higher relative value per share than under the non-IPO scenario.

Over time, as certainty developed regarding possible discrete events, including an IPO, the allocation methodology utilized to allocate our value transitioned from the Option Pricing Method, or OPM, which was utilized through July 2009, to the Probability Weighted Expected Return Method, or PWERM, which has been utilized since December 2009.

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Information regarding our stock option grants to our employees and certain non-employee members of our board of directors since January 1, 2009 is summarized as follows:

Date of issuance	Number of options granted	Exercise price	Common stock value	Option fair value ⁽¹⁾
March 19, 2009	1,462,500	\$ 1.93	\$ 1.93	\$ 0.89
April 21, 2009	43,000	\$ 1.93	\$ 1.93	\$ 0.90
May 19, 2009	40,000	\$ 1.93	\$ 1.93	\$ 0.91
June 10, 2009	505,000	\$ 2.82	\$ 2.82	\$ 1.36
July 21, 2009	206,000	\$ 2.82	\$ 2.82	\$ 1.31
July 24, 2009	330,000	\$ 2.82	\$ 2.82	\$ 1.32
December 15, 2009	986,000	\$ 4.25	\$ 4.25	\$ 1.94
February 3, 2010	2,203,555	\$ 4.25	\$ 4.25	\$ 2.00
February 17, 2010	1,095,000	\$ 4.25	\$ 4.25	\$ 2.00
February 22, 2010	750,000	\$ 4.25	\$ 4.25	\$ 2.01
June 8, 2010	947,500	\$ 5.42	\$ 5.42	\$ 2.77
June 9, 2010	200,000	\$ 5.42	\$ 5.42	\$ 2.77
July 8, 2010	74,500	\$ 6.37	\$ 6.37	\$ 3.32
July 19, 2010	573,000	\$ 6.37	\$ 6.37	\$ 3.32
July 29, 2010	360,000	\$ 6.37	\$ 6.37	\$ 3.32
August 4, 2010	218,583	\$ 6.71	\$ 6.71	\$ 3.50
August 12, 2010	500,000	\$ 6.71	\$ 6.71	\$ 3.50

(1) Option fair value determined using the Black-Scholes option pricing model using the input assumptions outlined above. The intrinsic value of all outstanding options as of June 30, 2010 was \$ million based on the estimated value of \$ per share, the midpoint of the planned range of this offering.

We granted stock options with exercise prices between \$4.25 and \$6.71 per share during 2010 while stock options with exercise prices between \$1.93 and \$4.25 per share were granted during 2009. No single event caused the valuation of our common stock to increase or decrease from January 2009 to August 2010, rather, it has been a combination of the following factors that led to the changes in the fair value of the underlying common stock.

March 2009 to May 2009. After a period of significant volatility in the U.S. and global capital markets during the third and fourth quarters of 2008, U.S. capital market conditions began to stabilize and recover in early 2009. During this time period, we introduced our SMRT technology and began to successfully manufacture key aspects of our system consumables in-house. Although the progression towards a commercial product continued to track to established timeframes, the depth and residual impacts of the economic turmoil of 2008, coupled with an inactive private capital market during early 2009, required us to reassess our potential exit scenarios, which had a material adverse effect on our value conclusions when compared to prior periods.

In deriving our enterprise value during the period, we applied a 65% weighting towards values derived using a market approach and 35% to those using an income approach based on discounted cash flows. In applying the OPM to the concluded value during this period, the expected term of our equity of 2.8 years was based on the weighted average time to liquidity of several assumed liquidity events. The volatility was based on the annualized average daily volatility over the expected term for our peer companies and was determined to be 56%. The risk-free interest rate was 0.84%, based on U.S. Treasury Securities corresponding to the expected term. Based on this information, we determined the total value of each security. We applied a discount of 33% for lack of marketability to the value of the common stock based upon a protective put calculation using the same assumptions as those used for the OPM allocation. For options granted during this period, we estimated the fair value of our common stock to be \$1.93 per share compared to the previous estimate of \$3.48 per share in December 2008.

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June 2009 to July 2009. Between June 2009 and July 2009, the weak recovery of the U.S. economy continued and, although signs of stability were becoming evident, access to private and public capital remained challenging. During this period, however, enterprise values of our publicly-traded peers outperformed the broader market. Our operational and development progress continued as expected and internal commercial launch timelines remained on schedule.

In deriving our enterprise value during the period, we applied a 65% weighting towards IPO scenarios occurring during 2010 and 2011 and 35% to remaining a private operating company. In applying the OPM to the concluded value during this period, the expected term of our equity of 2.7 years was based on the weighted average time to liquidity of several assumed liquidity events. The volatility was based on the annualized average daily volatility over the expected term for our peer companies and was determined to be 50%. The risk-free interest rate was 1.4%, based on U.S. Treasury Securities corresponding to the expected term. Based on this information, we determined the total value of each security. We applied a discount of 29% for lack of marketability to the value of the common stock based upon a protective put calculation using the same assumptions as those used for the OPM allocation. For options granted during this period, we estimated the fair value of our common stock to be \$2.82 per share.

December 2009 to February 2010. Between December 2009 and February 2010, the U.S. economy and U.S. capital markets began to stabilize. During the period leading up to December 2009, our peer group underperformed the market and experienced significant value declines as evidenced by decreases in the trading prices of their stocks. As a result, certain market multiples used as assumption inputs into our valuation models decreased. During this time period, however, we identified and entered into sales agreements with customers for our initial nine limited production release units of the PacBio RS instrument with expected deliveries commencing during mid-2010. We also continued to make progress in developing our full commercial release units. The combination of these factors supported our improved outlook regarding the fair value of our common stock under various IPO scenarios.

As noted previously, the OPM is preferred when future outcomes are difficult to predict and the PWERM becomes useful when discrete future outcomes become more predictable. During the period between July and December 2009, when the Board of Directors did not make valuation determinations or grant options, the range of discrete events, specifically IPO scenarios, became fairly well established, therefore the PWERM was utilized to determine the fair value of our common stock. The increase in the probability of a liquidity event from prior valuations was primarily related to commencement of sales and marketing operations and entering into sales agreements with customers for our instrument. The PWERM allocation method used a risk-adjusted discount of 31% based upon an adjusted capital asset pricing model, or adjusted CAPM, a marketability discount to specified events of 17% to 25% based on the average estimated time to each event ranging from 0.95 to 4.1 years. The expected outcomes were weighted 70% towards IPO scenarios occurring during late 2010 and through 2011, valued using the market approach, and 30% to remaining a private operating company, valued using the income approach. For options granted during this period, we estimated the fair value of our common stock to be \$4.25 per share.

June 2010. During June 2010, the equity markets demonstrated modest weakness as the broader markets and the stock prices of our peer companies declined in May and into June. However, through June, we secured multiple orders for the full commercial release of the PacBio RS, as well as an order for an additional limited production release unit.

The PWERM allocation method used an adjusted CAPM discount rate of 27%, a marketability discount to specified events of 9% to 25% based on the average estimated time to each event ranging from 0.53 to 4.7 years. The expected outcomes were weighted 88% towards IPO scenarios occurring during late 2010 and through 2011 and 12% to remaining a private operating company. For options granted June 3, 2010, we estimated the fair value of our common stock to be \$5.42 per share.

July 2010. During late June and early July 2010 the U.S. capital markets and the trading prices of our peer companies demonstrated modest stability. During this period, we completed our Series F convertible preferred stock financing raising a total of \$108.8 million. During July we also shipped three limited production release

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units to customers and commenced installation and testing of two of these units at customer locations. Finally, during July we conducted our IPO organizational meeting, which impacted our probability weightings regarding the timing of the IPO.

The PWERM allocation method used an adjusted CAPM discount rate of 26%, a marketability discount to specified events of 8% to 26% based on the average estimated time to each event ranging from 0.39 to 4.6 years. The expected outcomes were weighted 90% towards IPO scenarios occurring during late 2010 and through 2011 and 10% to remaining a private operating company. For options granted during July 2010, we estimated the fair value of our common stock to be \$6.37 per share.

August 2010. During mid- to late-July 2010, the U.S. capital markets weakened and, as a result, certain equity values and multiples of our peer public companies on which we base certain valuation calculations declined. The value we achieved as a company through research and commercial milestones more than offset the general declines in the markets and our peer companies. Specifically, during the first week of August, our first limited production release unit of the PacBio RS was accepted by a customer while additional units were being installed at customer sites.

The PWERM allocation method used an adjusted CAPM discount rate of 25%, a marketability discount to specified events of 7% to 27% based on the average estimated time to each event ranging from 0.30 to 4.5 years. The expected outcomes were weighted 90% towards IPO scenarios occurring during late 2010 and through 2011 and 10% to remaining a private operating company. For options granted during August 2010, we estimated the fair value of our common stock to be \$6.71 per share.

As noted above, our board of directors estimated the fair value of our common stock during these periods. We believe that the composition of our board of directors resulted in a fair and reasonable view of the stock value and, together with the board of directors' cumulative knowledge of, and experience with, similar companies, resulted in a fair valuation of our common stock.

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 2007, 2008 and 2009 was \$0.2 million, \$0.3 million and \$0.4 million, respectively. Stock-based compensation expense of \$0.1 million and \$0.6 million was recorded for the six-month periods ended June 30, 2009 and 2010, 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 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.

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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 Facility Financing and Debt Obligations in the Notes to Financial Statements of this prospectus.

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 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, 2009, we had a full valuation allowance against all of our deferred tax assets. At December 31, 2009, we had a full valuation allowance against all of

our deferred tax assets which totaled \$74.0 million, including net operating loss carryforwards and research and development tax credits of \$60.5 million and \$7.6 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, 2007, 2008, and 2009, our total unrecognized tax benefits were \$0.9, \$2.0, and \$3.9 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.

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

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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 Six-month Periods Ended June 30, 2009 and 2010*

	Six-month periods ended June 30, 2009 2010		Increase/ (decrease)	% Increase/ (decrease)
	(unaudited)			
	(in thousands, except percentages)			
Revenue	\$	\$ 1,174	\$ 1,174	
Research and development	30,090	52,406	22,316	74%
Sales, general and administrative	5,338	11,717	6,379	120%
Loss from operations	(35,428)	(62,949)	27,521	78%
Interest income (expense), net	327	(35)	(362)	(111)%
Other income (expense), net	(10)	(55)	45	450%
Net Loss	(35,111)	(63,039)	27,928	80%
<i>Revenue</i>				

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.

Research and Development Expense

The \$22.3 million increase in research and development expense was driven primarily by a \$12.3 million increase to laboratory and equipment expense, including prototypes, a \$6.7 million increase in personnel-related expense from increased headcount and an increase in facility and information technology expense of \$1.1 million. Research and development expense included stock-based compensation expense of \$1.1 million and \$2.5 million during the six-month periods ended June 30, 2009 and 2010, respectively.

Sales, General and Administrative Expense

The \$6.4 million increase in sales, general and administrative expense was driven primarily by a \$3.4 million increase in personnel related expense resulting from increased headcount, a \$1.5 million increase in customer application, demonstration and marketing initiatives and a \$1.2 million increase in equipment expense and depreciation. Furthermore, sales, general and administrative expense included stock-based compensation expense of \$0.3 million and \$1.2 million during the six-month periods ended June 30, 2009 and 2010, respectively.

Interest Income (Expense), Net

The decrease in interest income was due primarily to lower investment balances and lower interest rates on our investments. In addition we recorded interest expense as a result of the financing obligation under a lease agreement.

Table of Contents*Other Income (Expense), Net*

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

Comparison of the Years Ended December 31, 2008 and 2009

	Years ended December 31,		Increase/	% Increase/
	2008	2009	(decrease)	(decrease)
	(in thousands, except percentages)			
Revenue	\$ 901	\$ 135	\$ (766)	(85)%
Research and development	37,997	75,879	37,882	100%
Sales, general and administrative	7,713	12,326	4,613	60%
Loss from operations	(44,809)	(88,070)	43,261	97%
Interest income (expense), net	1,157	451	(706)	(61)%
Other income (expense), net	(102)	(84)	(18)	(18)%
Net Loss	(43,754)	(87,703)	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 \$1.2 million and \$2.3 million during 2008 and 2009, respectively.

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 a significant increase in 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 \$0.4 million and \$0.7 million during 2008 and 2009, respectively.

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.

Table of Contents*Comparison of the Years Ended December 31, 2007 and 2008*

	Years ended December 31, 2007	2008 (in thousands, except percentages)	Increase/ (decrease)	% Increase/ (decrease)
Revenue	\$ 2,163	\$ 901	\$ (1,262)	(58)%
Research and development	19,216	37,997	18,781	98%
Sales, general and administrative	6,338	7,713	1,375	22%
Loss from operations	(23,391)	(44,809)	21,418	92%
Interest income (expense), net	1,940	1,157	(783)	(40)%
Other income (expense), net	(67)	(102)	35	52%
Net loss	(21,518)	(43,754)	22,236	103%
<i>Revenue</i>				

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 \$1.3 million decrease in revenue realized was due to a reduction in the amount of awarded government grants in 2008 as compared to 2007.

Research and Development Expense

The \$18.8 million increase in research and development expense was driven primarily by a \$10.3 million increase in personnel related expense resulting from increased headcount, a \$4.4 million increase in prototype-related expenditures, equipment and development supplies, a \$2.3 million increase in information technology and facility expense and a \$0.9 million increase in contract services and other professional services. Research and development expense included stock-based compensation expense of \$0.4 million and \$1.2 million during 2007 and 2008, respectively.

Sales, General and Administrative Expense

The \$1.4 million increase in sales, general and administrative expense was driven primarily by a \$1.9 million increase in personnel related expense resulting from increased headcount primarily in operations and recruiting activities and a \$0.2 million increase in trade show and promotional expense related to increased public relations and market research activities, offset by a \$1.0 million decrease in professional services primarily driven by non-recurring legal fees. Sales, general and administrative expense included stock-based compensation expense of \$0.2 million and \$0.4 million during 2007 and 2008, respectively.

Interest Income (Expense), Net

The decrease in interest income was due primarily to lower investment balances and lower interest rates on our investments.

Other Income (Expense), Net

The change in other income (expense), net was insignificant.

Liquidity and Capital Resources

Since our inception, and as of June 30, 2010, we have financed our operations primarily through an aggregate of \$356.0 million from private placements of convertible preferred stock.

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As of June 30, 2010, we had cash, cash equivalents and investments of \$138.8 million and no debt obligations. For the six-month period ended June 30, 2010, we closed private placements of convertible preferred stock with net proceeds of \$97.9 million.

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

	As of December 31,		June 30,
	2008	2009	2010
		(in thousands)	(unaudited)
Working capital	\$ 102,224	\$ 85,326	\$ 123,896
Cash, cash equivalents and investments	106,051	92,735	138,756

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

	Years ended December 31,			Six-month periods ended	
	2007	2008	2009	2009	2010
			(in thousands)	(unaudited)	
Net cash used in operating activities	\$ (16,732)	\$ (38,303)	\$ (74,838)	\$ (29,374)	\$ (49,595)
Net cash provided by (used in) investing activities	(18,338)	(10,393)	18,594	160	(48,227)
Net cash provided by (used in) financing activities	(225)	119,927	67,014	(394)	98,734

During the years ended December 31, 2007, 2008 and 2009 and in the six-month period ended June 30, 2010, we used \$3.0 million, \$5.7 million, \$5.2 million and \$3.0 million in cash, respectively, to fund capital expenditures. We currently anticipate making significant 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 the net proceeds from this offering, 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. 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 ownership of our stockholders will be diluted and the new equity securities may have priority rights over existing stockholders.

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 \$16.7 million, \$38.3 million and \$74.8 million for the years ended December 31, 2007, 2008 and 2009, respectively and \$29.4 million and \$49.6 million for the six-month periods ended June 30, 2009 and 2010, respectively.

Cash used in operating activities of \$49.6 million for the six-month period ended June 30, 2010 reflected a net loss of \$63.0 million, partially offset by aggregate non-cash charges of \$6.3 million and a net change of \$7.1 million in our net operating assets and liabilities. Non-cash charges primarily included \$2.3 million of depreciation and \$4.0 million in stock-based compensation. The net change in our operating assets and liabilities was primarily a result of the increase in accrued expenses and other current liabilities of \$5.5 million.

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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.

Cash used in operating activities of \$16.7 million in 2007 reflected a net loss of \$21.5 million, partially offset by aggregate non-cash charges of \$3.2 million and a net change of \$1.6 million in our net operating assets and liabilities. Non-cash charges primarily included \$1.6 million of depreciation and \$1.7 million of stock-based compensation. The net change in our operating assets and liabilities was primarily a result of the increase in accounts payable of \$1.4 million.

Cash Flows From Investing Activities

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

For the six-month period ended June 30, 2010, cash used in investing activities was \$48.2 million as a result of \$45.2 million in net investment purchases and \$3.0 million of capital expenditures.

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.

In 2007, cash used in investing activities was \$18.3 million as a result of \$15.3 million in net investment purchases and \$3.0 million of capital expenditures.

Cash Flows From Financing Activities

For the six-month period ended June 30, 2010, cash provided by financing activities was \$98.7 million, primarily as a result of the receipt of \$97.9 million from our sale 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.

In 2007, cash used in financing activities was \$0.2 million, primarily as a result of net repayments on our debt of \$0.4 million.

Table of Contents**Contractual Obligations, Commitments and Contingencies**

The following table provides summary information concerning our future contractual obligations as of June 30, 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⁾	\$ 7,111	\$ 2,586	\$ 2,543	\$ 1,920	\$ 62
Facility financing obligation	2,029	333	852	844	
Total contractual obligations	\$ 9,140	\$ 2,919	\$ 3,395	\$ 2,764	\$ 62

(1) Maintenance, insurance, taxes and contingent rent obligations are excluded. See our financial statements and related notes included elsewhere in this prospectus for a discussion of our operating leases.

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 on the balance sheet as of June 30, 2010. See our financial statements and related notes included elsewhere in this prospectus for a discussion of this commitment.

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 minimum royalty and license maintenance fees. Pursuant to the terms of the agreements, future license maintenance fees and minimum royalty payments amount to \$0.3 million for 2010, and \$0.4 million for each of 2011, 2012 and 2013 and 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 milestone fees 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

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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.

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.

Recent Accounting Pronouncements

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.

In April 2010, the FASB issued an accounting standards update which provides guidance on the criteria to be followed in recognizing revenue under the milestone method. The milestone method of recognition allows a vendor who is involved with the provision of deliverables to recognize the full amount of a milestone payment upon achievement, if, at the inception of the revenue arrangement, the milestone is determined to be substantive as defined in the standard. The guidance is effective on a prospective basis for milestones achieved in fiscal years and interim periods within those fiscal years, beginning on or after June 15, 2010. The adoption of this guidance is not expected to have a material impact on our financial statements.

Table of Contents**BUSINESS****Overview**

We develop, manufacture and market an integrated platform for genetic analysis. We have developed an approach 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 called 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 research community with a new tool for investigating basic biochemical processes such as DNA synthesis. We believe our SMRT technology has the potential to advance scientific understanding by providing a window into biological processes that has not previously been open.

In the past fifteen years, there have been a number of important advances in the understanding of biological systems, including the initial characterization of the cellular blueprints, or genomes, of humans and a number of other organisms. These discoveries which were expected to herald a new age in science and medicine have yet to deliver on their promise, due in part to the limitations of currently available life science tools that rely on averages and aggregates. These techniques often mask potentially important sources of variation that are believed to underlie diseases such as cancer. We believe our technology addresses these limitations and may lead to important new advances in the understanding of biological systems.

Our initial focus is on the DNA sequencing market where we have developed and introduced a third generation sequencing platform, the PacBio *RS*. We believe that the PacBio *RS*, which uses our proprietary SMRT technology, 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, lower throughput, 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 three chemical reagent kits. Customers use these reagent kits to format and sequence their DNA samples. The Template Prep Kit includes ligase and restriction enzymes, the Binding Kit includes our DNA polymerase and the Sequencing Kit includes our phospholinked nucleotides. The system is designed to be integrated into existing laboratory workflows and information systems. Customers that have placed orders for our products include research institutions and commercial companies that plan to use the PacBio *RS* for clinical, basic and agricultural research, drug discovery and development, biosecurity and bio-fuels. Our customers are also interested in a number of other potential applications, including molecular diagnostics, food safety and forensics, which may require us to enhance the capabilities of our current products or develop additional products. To date, we have neither commercially launched nor generated any revenue from our products.

We believe that our SMRT technology has the potential to impact scientific study beyond DNA sequencing. We, and our scientific collaborators, have published a number of peer-reviewed articles in journals including *Science*, *Nature* and *Nature Methods* highlighting the power and potential applications of the SMRT platform. Potential applications that have been demonstrated include the study of chemical and structural modifications of DNA and the processing of RNA and proteins although these applications will not be available at commercial launch of the PacBio *RS*. We plan to provide these additional capabilities through enhancements to software and consumables without modifications to the PacBio *RS*.

Evolution of Biology*Classical Biology*

Genetic inheritance in living systems is conveyed through a naturally occurring information storage system known as deoxyribonucleic acid, or DNA. DNA stores information in a linear sequence of the chemical bases adenine, cytosine, guanine and thymine, represented by the symbols, A, C, G and T. These bases are attached to a repeating linear chain made up of alternating sugar and phosphate segments. Inside living cells, these chains

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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 an RNA message or mRNA. The mRNA carries the same sequence as the DNA, except that the DNA base thymine is replaced by uracil, so that the RNA alphabet is A, C, G and U. These messages are taken to the cellular protein factories, called ribosomes, for translation into proteins. These proteins go on to play crucial roles in the structure and function of the cell, including the regulation and execution of transcription and translation. The characterization of these events as a simple multi-step linear process from DNA to RNA to protein has been referred to as the Central Dogma of Molecular Biology and has formed the backbone of classical biology.

The linear process implied by the Central Dogma led to the development of tools that focused on isolated elements of living systems. These tools collect data reflecting averages of isolated events at static points in time, missing many of the complex dynamics and biological contexts critical to a full understanding of biological processes. Therefore, the study of biology is predisposed towards incomplete and deterministic pictures of biological systems.

Based on the Central Dogma, a common expectation developed that once the full genetic code of a human was available, the mechanisms of human biology would be substantially revealed. The International Human Genome Project, designed to map the human genome, took 13 years at a cost of over \$3 billion and resulted in only approximately 92% coverage of the genome at its conclusion in 2004. The project resulted in many important insights regarding human biology, including a reduction in the number of estimated genes in the human genome from 100,000 or more to approximately 23,000. The data analysis techniques available at the time were able to identify single-nucleotide polymorphisms, or SNPs, places in the genome where individuals commonly differ by a single letter. This resulted in a view that there is a reference genome approximating all humans, with SNPs representing the dominant source of genetic variation. This view fostered an expectation that a new era of diagnosing and treating disease would emerge.

However, this promise has not been delivered due to our incomplete understanding of biological mechanisms underlying human disease. With the expectation that knowledge of the genome would guide the process towards safe and effective drugs, the pharmaceutical industry has spent billions of dollars on high-throughput screening of potential drug compounds without a significant increase in research productivity. Today, biological science remains largely unable to effectively determine which proteins should be targeted in order to treat disease.

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.

The genomics research community has realized that a single reference sequence is not sufficient to decipher the inner workings of life. This led to a new type of study, commonly called genome-wide association studies, or GWAS, in which the genomes of large numbers of individuals are checked at known SNPs, and these findings are correlated with specific conditions, such as disease. While these studies have advanced our general understanding, in most cases they have not improved diagnosis and treatment as hoped. The correlations found by these methods are generally not large enough to be useful in detecting or treating human disease. Further, the research community has developed a deeper appreciation for the importance of additional sources of genomic variation, including chemical, structural and functional genomic modifications.

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Future Biology

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 GWAS 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.

Differences between genomes at different positions can be highly interactive, for example, a mutation that increases lifetime risk of cancer in one genomic context may decrease risk in another context. While the two copies of the 23 chromosomes we inherit from our parents are enormously important in determining who we are, our genomes continue to change as we age. Understanding the genetic makeup of an individual, including mutations that take place after conception, is key to understanding and treating diseases. For example, the genomes of cells within a particular individual's tumor may show significant variation from one cell to the next and from one time-point to the next.

Recent discoveries have highlighted additional complexities in the building blocks of DNA (A, C, G and T) and RNA (A, C, G and U), including the presence of additional bases. It has long been known that in humans and many other multicellular organisms the C 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.

It is now understood that the role of RNA as detailed in the Central Dogma requires significant revision. The RNA components of the cell, which were originally thought only to relate to the production of proteins, are now known to play important regulatory roles. Numerous functional elements have been identified and located in regions far from any protein-coding sequence, many with no indications of how they might function. Not surprisingly, significant discrepancies have been found between the levels of mRNAs and the levels of the proteins for which they code. This is caused by regulation of the translation process that takes place after the mRNA is made. For example, binding of short RNA segments called micro-RNAs or miRNAs to mRNA have been shown to inhibit translation of their mRNA target.

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 comprising sample preparation, physical sequencing and re-assembly. The first step of sample preparation is to break the target genome into multiple small fragments.

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Depending on the amount of sample DNA, these 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. The ability to use sequence-based information is contingent not only on assembly, but the accuracy of the assembled sequence. There are two principal forms of accuracy that are commonly cited, referred to as raw read accuracy and finished or consensus accuracy. The former can be a platform specific performance metric while consensus accuracy is critical to successful reassembly.

First Generation Sequencing

First generation sequencing, also called 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. This 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 addition to introducing errors in the sequence, the process of amplification increases the complexity and time associated with sample preparation.

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 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.

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Pacific Biosciences Solution The Third Generation

We have developed a technology platform that enables single molecule, real-time, or SMRT, detection of biological processes. Our SMRT technology harnesses the natural activity of key enzymes involved in the synthesis and regulation of biomolecules including DNA, RNA and protein. 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, including short readlengths, limited flexibility, long time to result, lower throughput, complex sample preparation and risk of amplification bias, and may also enable other types of 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 harnesses the natural process of DNA replication, which in nature is a highly efficient and accurate process. The enzyme responsible for replicating DNA in nature is called 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.

Our SMRT technology enables the observation of DNA synthesis as it occurs in real time. To overcome the challenges inherent in observing an enzyme that is 15 nanometers, or nm, in diameter running in real time, we developed 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 applied the same principle that operates in the metallic screen of a microwave oven door. In a microwave oven, the screen is perforated with holes that are much smaller than the wavelength of the microwaves. Because of their relative size, the holes prevent the much longer microwaves from passing through and penetrating the glass. However, the much smaller wavelength visible light is able to pass through the holes in the screen, allowing food to be visible. We have reduced this same principle to the nanoscale and we call our innovation a zero-mode waveguide, or ZMW.

A ZMW is a hole, tens of nanometers in diameter, fabricated in a 100nm metal film deposited on a glass substrate. 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 exponentially decays as it enters the ZMW. Therefore, by shining a laser through the glass 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 glass surface 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. Diffusion at the nanoscale is incredibly fast. Within microseconds, labeled nucleotides

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travel down into the ZMW, surround the DNA polymerase, then diffuse back up and exit the hole. 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.

Our DNA sequencing is performed on proprietary SMRT Cells, each having an array of approximately 75,000 ZMWs. Each ZMW is capable of containing a DNA polymerase loaded with a different strand of DNA sample. As a result, the SMRT Cell enables the potential detection of approximately 75,000 single molecule sequencing reactions in parallel. Currently, our immobilization process randomly distributes polymerases into ZMWs across the SMRT Cell, resulting in only approximately one-third of the ZMWs being available for use.

Phospholinked Nucleotides

Previous labeling technologies for nucleotides attach a fluorescent label to the base of the nucleotide, which is incorporated into the DNA strand. This is problematic for any system attempting to observe DNA synthesis in real time because the dye's large size relative to the DNA can interfere with the activity of the DNA polymerase. In second generation sequencing, a DNA polymerase can incorporate only a few base-labeled nucleotides before it halts. 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.

Putting the Three Innovations Together

Our three innovative technologies work together to allow researchers to sequence long reads of DNA in minutes. As discussed above, the DNA polymerase is immobilized on the floor of the ZMW. Phospholinked nucleotides are introduced into the SMRT Cell from above. As the phospholinked nucleotides diffuse through the bottom 30nm of each ZMW in the SMRT Cell, the PacBio RS detects the presence of free nucleotides as low intensity flashes of light. When the DNA polymerase encounters the nucleotide complementary to the next base in the template, it is incorporated into the growing DNA chain. During incorporation, the DNA polymerase holds the nucleotide for tens of milliseconds, orders of magnitude longer than the average diffusing nucleotide. While held by the polymerase, the fluorescent label emits colored light. The PacBio RS detects this as a higher intensity flash of light whose color corresponds to the base identity, which is recorded. Upon incorporation, the fluorescent label is cleaved and the signal immediately returns to baseline and the process repeats, with the DNA polymerase continuing to incorporate multiple bases per second.

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SMRT Sequencing

The top graphic is an illustration of DNA sequencing. The bottom graphic represents the output of the PacBio RS identifying the incorporation of nucleotides in a growing DNA strand.

Step 1: As nucleotides diffuse into the ZMW, low intensity flashes of light are generated.

Step 2: When the DNA polymerase encounters the nucleotide complementary to the next base in the template, the DNA polymerase holds the nucleotide for tens of milliseconds and the fluorescent label emits a higher intensity flash of light whose color corresponds to the base identity, which is recorded as an A in the graphics above.

Step 3: Upon incorporation of the nucleotide, the fluorescent label is cleaved and signal returns to baseline.

Step 4: The process repeats, and in this illustrative example the nucleotide being incorporated is a T.

Step 5: Following incorporation of the next nucleotide, the next fluorescent label is cleaved and signal returns to baseline again.

SMRT Sequencing Advantages

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

Single molecule, real-time analysis. SMRT technology harnesses the power of the DNA polymerase to enable single molecule, real-time sequencing. 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. In addition, our platform does not require the routine PCR amplification needed by most second generation sequencing systems thereby avoiding systematic amplification bias.

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. Most second generation technologies require higher coverage to compensate for short readlengths. However, even with high coverage, short readlengths are difficult to assemble, especially in highly repetitive areas of the genome. In addition, 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

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large-scale rearrangements as observed in cancer. We believe that the long readlengths produced by our SMRT technology may allow insights into biology that are not possible with existing technologies.

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

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target polymerase speeds of one to three bases per second. This speed enables the research community to ask and answer questions much faster than with 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.

Ease of use. We believe that 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. Sample preparation processes for second generation technology often involve costly additional capital equipment, reagents, supplies and physical space. This process can take multiple days. 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. We call this granularity, and it results from our flexible consumables format. The ability to run a single SMRT Cell, or batch multiple SMRT Cells in a single run, provides flexibility in experiment design and implementation.

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 presence or absence of a methyl group can determine whether or not a gene is expressed in a particular cell, tissue or organism. The impact of such chemical modification of DNA on the expression of genes has been hypothesized to play a role in many diseases, including cancer. Importantly, it has been shown that changes in kinetics which can be detected automatically by the PacBio RS, may reflect the presence of DNA methylation.

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 changes to the hardware.

The PacBio RS is compatible with existing customer infrastructure, from sample preparation to biological results and analysis. This includes our SMRTbell sample preparation protocol, remote experimental management, touchscreen instrument operation, integration with preferred IT infrastructures and backwards-compatibility with existing informatics pipelines. Together, this results in quick system setup times, fast scaling to multi-unit configurations and short turnover time between experiments. We believe these factors will result in a new paradigm for sequencing experiments from days and weeks to minutes and hours.

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

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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. For a description of the process from sample preparation to sequencing results using the PacBio *RS*, see *Using the PacBio RS* below. The PacBio *RS* has been designed to allow for performance improvements without an upgrade or replacement of the instrument hardware. These performance enhancements will be delivered through software upgrades and new consumables. A comprehensive informatics tools suite that enables users to generate finished sequence data is also included. The list price for the PacBio *RS* will be \$695,000 in the United States.

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.

We offer three 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.

Using the PacBio RS

The PacBio *RS* delivers a complete product solution from sample preparation to biological results. The instrument has the capability for multiple sequencing protocols, enabling a high degree of flexibility in experimental design.

Standard sequencing. The standard SMRT sequencing protocol is designed to generate single pass long reads. The protocol uses long insert lengths so that the polymerase can continuously synthesize along a single strand. As with all protocols, this process runs in parallel across thousands of ZMWs in a single SMRT Cell at the same time. This protocol has utility for a range of both resequencing and *de novo* applications. Our system achieves consensus accuracy of 99.99% which is commensurate with leading second generation sequencing systems.

Circular consensus sequencing. The PacBio *RS* has the capability for circular consensus sequencing. The circular consensus sequencing protocol uses a circular DNA template which enables multiple reads across the same sequence to achieve 99.99% accuracy at single molecule resolution from a single DNA strand. Furthermore, this approach provides reads on both the forward and reverse strands of a double stranded template. This method offers potential advantages for the discovery and confirmation of rare variants.

Strobe sequencing. The PacBio *RS* also has the capability for strobe sequencing. Using this protocol, the physical coverage and effective readlength of the system can be increased by strobing the illumination on and off. When the illumination is on, sequence data is collected, but when the illumination is off, the polymerase continues to synthesize in the dark at a predictable speed for thousands of bases. After a user-defined interval, the illumination can be turned back on and the system can resume collecting data. Multiple sub-reads at varying sequence advance lengths can be generated from a single molecule. The length of the strobe sub-reads and advances can be controlled dynamically as a run parameter, thereby eliminating the need to create multiple libraries of different sizes. This method will be useful for scaffolding, or mapping a series of short fragments on a longer DNA strand, genomic assembly and identifying and resolving structural variation.

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Combining sequencing modes. The system's flexibility also offers the ability to approach a problem in multiple ways. For example, users may first want to scaffold the sequence using the strobe sequencing protocol, then generate long linear single molecule reads, and finally, apply circular consensus sequencing to identify rare sequence variants.

The PacBio *RS* requires limited manual intervention. The illustration below outlines the flow of the process from sample preparation to sequencing results.

The sample preparation protocol employs simple, standard molecular biology techniques and can be completed in hours. The same protocol can be used with a variety of sample types and can generate a range of library sizes. The Template Preparation Kit is used to convert DNA into our SMRTbell library format. The Binding Kit is then used to bind this library to the polymerase in preparation for sequencing.

Customers design, manage and monitor experiments from their desktop. This experimental information can be integrated with internal laboratory information management systems, or LIMS, or other tracking systems.

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Instrument operation occurs through a touchscreen interface, *RS Touch*, and requires minimal user intervention. The instrument is both an automated liquid handling and detection platform. Customers load SMRT Cells and the sequencing kit components directly into two drawers on the instrument, from which point dispensing and handling are automated by the robotic station. Barcode tracking provides efficient management of samples and reagents.

Once the sequencing reaction has been initiated, the high performance optics monitor the thousands of ZMWs in real time. Throughout the sequencing process, the *RS Touch* provides feedback on the status of the PacBio *RS*, its contents and the experimental progress.

Concurrent with the sequencing process, base calling and quality assessment are performed through the Blade Center, the computational brain of the PacBio *RS*. Primary analysis data can be streamed directly to the secondary analysis system as well as visualized. Secondary analysis provides data-rich reports for the user, including informative quality and application-specific metrics. Users can then interact visually with the data at all relevant levels, from the genome view to individual SNPs.

We are committed to providing users with access to the right types of high-performance computing environments to not only store and organize the data, but to also interact with and analyze the data on different levels. These informatics solutions are designed to efficiently integrate with on-premises or cloud-based LIMS systems making these solutions accessible not only to high-end informatics researchers, but also to biologists and clinicians.

Developer tools enable seamless integration with existing bioinformatics pipelines. All data files are directly accessible, giving the user flexibility to perform further analysis through third-party software or share data with collaborators. To maximize the flexibility and functionality for all users, all of the secondary analysis algorithms are open source.

Market Opportunity

Despite the limitations of currently available sequencing platforms, 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 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 accelerate 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:

Define the future of biological analysis based on SMRT technology. Our SMRT technology provides a window into biological processes that has not previously been available. We have and will continue to communicate the benefits and advantages of our SMRT technology platform through our commercial and marketing activities. In addition, we will continue to pursue publication of

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biological insights using our SMRT technology in top-tier scientific, peer-reviewed journals. For example, a recent publication in Nature demonstrated the broad applicability of the SMRT detection technology by enabling new, high resolution insights into ribosome function and composition during translation at physiological concentrations of transfer RNAs. We plan to continue to develop the applications of our SMRT technology in the fields of DNA, RNA and protein biology.

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. Customers that have placed orders for our products include research institutions and commercial companies that plan to use the PacBio *RS* for clinical, basic and agricultural research, drug discovery and development, biosecurity and bio-fuels. Our customers are also interested in a number of other potential applications, including molecular diagnostics, food safety and forensics, which may require us to enhance the capabilities of our current products or develop additional products.

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. These performance enhancements will be delivered through software upgrades and new consumables. 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. We believe that our ability to offer performance improvements without requiring new hardware investment by our customers will increase the attractiveness of our products.

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 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 the secondary analysis algorithms are open source.

Future Commercial Applications

We believe that the power of SMRT detection extends beyond DNA sequencing to the detection and characterization of other fundamental biological functions. The ability of the SMRT technology to observe kinetic information of individual molecules provides the ability to detect nucleic acid variations, including detection of base modifications and the detection of binding of biomolecules to DNA. SMRT detection has been applied by researchers to directly observe, on a single molecule basis, transcription, reverse transcription, translation and ligand binding. Although these applications will not be available at the commercial launch of the PacBio *RS*, we plan to further develop them and, if successful, we may commercially introduce them in the future.

SMRT Kinetic Detection. SMRT analysis enables the observation of the kinetics of DNA and RNA synthesis. Kinetic analysis may permit detection of base modifications in DNA and RNA beyond simple methylation. These modifications, which are hypothesized to play an important role in diseases such as cancer,

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have not been systematically studied due to a lack of efficient tools. The analysis of synthesis kinetics is not limited to studies of molecular structure, but is also applicable to the detection of inter-molecular interactions, for example, detecting kinetic impacts of protein-DNA interactions. Both of these applications of the SMRT platform may have important applications in disease characterization, diagnosis and treatment.

SMRT Transcription. By replacing the DNA polymerase with an RNA polymerase, SMRT detection provides the ability to directly observe in real time the regulation of transcription of a gene into an RNA message, the first phase of protein expression. The combined power of direct observation of transcription and the sequence context that SMRT sequencing provides has the potential to replace present transcription assays and enable transcription analysis on a whole genome scale. It is possible that this process plays a role in diseases, such as cancer.

SMRT RNA Sequencing. By replacing the DNA polymerase with a reverse transcriptase in the ZMW, SMRT detection provides the ability to directly sequence RNA and observe kinetic data similar to that seen with DNA sequencing. Directly sequencing RNA may provide advantages over traditional methods including speed, longer readlengths and reduced errors into the determined sequence.

SMRT Translation. We have demonstrated the ability to observe protein translation in real time at the single molecule level by placing the ribosomal complex into the ZMW and attaching fluorescent tags to the molecules that escort the amino acids to the ribosome for protein production. It is understood that the levels of mRNA do not always correlate with the amounts of the corresponding proteins, due in part to RNA regulatory mechanisms such as miRNA binding. For this reason it is desirable to measure the levels of the many proteins as synthesized by the ribosome. As proteins represent an important target for therapeutics, understanding the dynamics of protein synthesis may be important for future drug discoveries.

SMRT Ligand Binding. The interaction between ligands, including drugs and their respective biological targets, referred to as ligand binding, is an important facet of basic science. Most current ligand binding analysis techniques detect average interactions over large populations of molecules and do not detect changes in the interactions in real time. This results in an inability to detect weak interactions, or detect multi-body interactions where individual components can be interacting on a transient basis. Because it detects individual molecular interactions, we believe the SMRT detection system can probe binding interactions that are far weaker than those detected by other techniques. Further, because of its real-time observation, it can detect binding events lasting only a few milliseconds. Given the importance of ligand binding to the drug discovery process and other potential commercial applications, this new application may offer significant advantages over traditional methods.

Marketing and Sales

We market our products through a direct sales force in North America and the United Kingdom. Our sales strategy involves the use of a combination of sales managers, sales representatives and field application specialists. As of June 30, 2010, we had six sales managers and sales representatives and five 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, including four with PhDs, 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.

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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 scheduled for early 2011. 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. As of September 15, 2010, we have shipped a total of seven PacBio *RS* limited production release instruments, and we intend to ship the remaining four later this year. Limited production release instruments are designed to provide early access to the technology, while we complete the research, development and testing required for full commercial release. Therefore, performance during the limited production release phase will not be equal to that of the system at commercial release. There will be a continuous evolution of these performance variables, including readlength and throughput, during the limited production release phase as we develop new versions of our software and consumables. During a testing period, which we expect to last at least through the end of 2010, we will be working with these customers to obtain feedback and plan to incorporate relevant improvements into the commercial release version of the PacBio *RS*. Generally, each customer is obligated to pay us a deposit after accepting a limited production release instrument, and is entitled to receive an upgrade to a commercial release version of the PacBio *RS*, at which time each customer will be obligated to pay the balance of their order and we will then recognize revenue. While we expect to deliver upgrades to all of these customers, we cannot provide assurance that we will succeed and recognize revenue from our limited production release customers.

Backlog

As of June 30, 2010, our backlog was approximately \$15 million. 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, however we do not expect to recognize revenue on any orders prior to December 31, 2010. Estimating the dollar value of backlog requires significant judgments and estimates. We may never ship these units or receive revenue from these orders, and our backlog may not be indicative of our future revenue. If our orders in backlog do not result in sales, our operating results will suffer.

Manufacturing

Our 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.

The manufacture of our instruments is complex involving a number of separate processes and components. Our manufacturing processes are detailed in written procedures and extensive testing and data collection is performed throughout the process. We have implemented quality control procedures to help assure that our

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products meet our specifications. We also use manufacturing process control software to help us ensure key processes are followed with a high degree of integrity.

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 June 30, 2010, we had five 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.

Our instruments are designed with remote diagnostics that generate automated alerts that will allow us to promptly initiate preventive maintenance or repair. We intend to establish an online customer portal and case management system to aid in the technical support of our instruments. We also intend to establish a contact center in each region to handle incoming inquiries via telephone, email or live chat.

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.

Our research and development group is comprised of eight departments, Biochemistry, Organic Chemistry, Surface Chemistry, Nanofabrication, Mechanical/Optical/Electrical Engineering, Software Engineering and Bioinformatics, Systems Integration and Single Molecule Sample Prep and Detection. Combined, these groups are responsible for the research and development of the various technologies needed to supply the basic chemistry components and protocols, reaction cells, instrument platform and the embedded and downstream software that are needed to prepare, process, detect, analyze and interpret single molecule, real-time data. Research and development expense incurred for these activities was \$19.2 million, \$38.0 million and \$75.9 million in 2007, 2008 and 2009, respectively. As of June 30, 2010, we had 208 scientists and engineers in our research and development group of which 146 have advanced degrees including 105 with PhDs.

We will continue to invest 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.

As of June 30, 2010, we own or hold exclusive licenses to 47 issued U.S. patents, 118 pending U.S. patent applications, six granted foreign patents and 138 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, 18 issued U.S. patents, six pending U.S. patent applications, one granted foreign patent and five 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 whereby the U.S. Government may disregard our exclusive patent rights under our license from Cornell 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. 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 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

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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., Oxford Nanopore Technologies Ltd. and Ion Torrent Systems Inc., which recently announced that it had entered into a definitive agreement to be acquired by Life Technologies Corporation.

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 June 30, 2010, we had 369 full-time employees. Of these employees, 208 were in research and development, 88 were in operations and program management, 43 were in sales and marketing and 30 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 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.

Table of Contents**Facilities**

Our corporate headquarters and manufacturing facilities are located in Menlo Park, California where we lease approximately 147,000 square feet of office, lab and manufacturing space. The schedule below summarizes our facilities as of September 15, 2010. We consider our manufacturing facilities sufficient to meet our current and planned operational requirements. 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
30,240	May 2011	Office/Lab
31,560	May 2011	Office/Lab
33,792	July 2015	Office/Training
22,267	September 2013	Manufacturing
29,371	April 2015	Manufacturing

Legal Proceedings

We are presently involved in a patent interference with Life Technologies Corporation, or Life, related to U.S. Patent No. 7,329,492, 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 this interference, it was determined that we are the senior party in the interference based upon an initially accorded priority date prior to that of the Life patent. The first phase concluded on December 1, 2009, when the parties presented oral arguments to the USPTO's Board of Patent Appeals and Interferences, or BPAI. As of July 31, 2010, no decision has yet been rendered by the BPAI on the parties' respective arguments.

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. While we cannot guarantee any outcome of this lawsuit, we intend to defend against these claims and argue that we do not infringe the claims of the asserted patents and that the claims of the asserted patents are invalid and unenforceable.

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

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The following table sets forth the names, ages and positions of our executive officers and directors as of June 30, 2010.

Name	Age	Position
Hugh C. Martin	56	Chairman, Chief Executive Officer and President
Susan K. Barnes	56	Senior Vice President and Chief Financial Officer
Stephen Turner, PhD	42	Chief Technology Officer
Michael Phillips	60	Senior Vice President Research and Development
William Ericson ⁽²⁾	51	Lead Independent Director
David Baltimore	72	Director
Brook Byers ⁽¹⁾⁽³⁾	64	Director
Michael Hunkapiller, PhD ⁽²⁾	61	Director
Randy Livingston ⁽¹⁾	56	Director
Susan Siegel ⁽²⁾⁽³⁾	50	Director
David Singer ⁽¹⁾⁽³⁾	47	Director

(1) Member of our audit committee

(2) Member of our compensation committee

(3) Member of our corporate governance and nominating committee

Executive Officers

Hugh C. Martin has served as our Chairman, Chief Executive Officer, President and a member of our board of directors since joining us in 2004. From 2003 to 2004, Mr. Martin was a chief executive officer coach at Kleiner Perkins Caufield & Byers. From 1998 to 2002, Mr. Martin was chairman, president and chief executive officer of ONI Systems, a high-speed optical telecommunications company he founded. Mr. Martin served on the board of directors of Infinera Corporation from July 2003 to June 2009. We believe that Mr. Martin possesses specific attributes that qualify him to serve as a member of our board of directors, including the perspective and experience he brings as our Chief Executive Officer and his experience as a seasoned executive with a 25-year track record managing companies bringing leading edge technologies to market and managing high growth businesses. Mr. Martin holds a B.S. degree in Electrical Engineering from Rutgers University.

Susan K. Barnes has served as our Senior Vice President and Chief Financial Officer since she joined us in February 2010. From 1997 to 2005, she was senior vice president, finance and chief financial officer of Intuitive Surgical, Inc. Ms. Barnes served on several boards of directors of public and private companies, including Northstar Neuroscience, Inc. from February 2006 to December 2009, where she also served as audit committee chair, and RAE Systems from September 2004 to May 2006, where she served as chair of the audit committee. Ms. Barnes holds an A.B. from Bryn Mawr College and an M.B.A. from the Wharton School, University of Pennsylvania.

Stephen Turner, PhD co-founded Pacific Biosciences in July 2000. Dr. Turner served as our President and Chief Executive Officer from the company's inception until March 2004, when he assumed his current role as our Chief Technology Officer. He served as a member of our board of directors from inception until July 2010. Prior to founding the company Dr. Turner contributed to the establishment of the Nanobiotechnology Center at Cornell University in January 2000. Dr. Turner holds a PhD in Physics from Cornell University. He received B.S. degrees in Applied Mathematics, Electrical Engineering and Physics from the University of Wisconsin, Madison.

Michael Phillips joined Pacific Biosciences in April 2005 as our Vice President of Product Development and since February 2010 has served as our Senior Vice President of Research and Development. Prior to joining

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us, Mr. Phillips held various management roles at Applied Biosystems spanning research and development, test, manufacturing operations and service support from 1986 to April 2005. His most recent position at Applied Biosystems was Director of Research and Development. Mr. Phillips earned a B.S. degree in Bacteriology from the University of California, Davis.

Directors

William Ericson has been a member of our board of directors since 2004 and has been appointed our Lead Independent Director. Mr. Ericson is a Managing Partner at Mohr Davidow Ventures, or MDV, a venture capital firm. He joined Mohr Davidow Ventures in 2000 after more than a decade of working closely with entrepreneurs to start and build innovative businesses in the role of lawyer, board member, entrepreneur and investor, and has led MDV's focus on personalized medicine investing since 2003. We believe that Mr. Ericson possesses specific attributes that qualify him to serve as a member of our board of directors, including his experience with multiple companies in the life sciences industry and his focus on companies with molecular diagnostic platforms that will enable the vision of personalized medicine. Mr. Ericson holds a B.S.F.S. from Georgetown University of Foreign Service and J.D. from Northwestern University School of Law.

David Baltimore, PhD has been a member of our board since September 2010. Since 2006, he has been President Emeritus and the Robert Andrews Millikan Professor of Biology at the California Institute of Technology, or Caltech. From 1997 to 2006, Dr. Baltimore served as President of Caltech. Prior to joining Caltech, Dr. Baltimore was a professor at the Massachusetts Institute of Technology, or MIT, and at The Rockefeller University where he also served as the President. He received the Nobel Prize in Medicine as a co-recipient in 1975 and the National Medal of Science in 1999. Dr. Baltimore is a member of the U.S. National Academy of Sciences as well as a member of the Royal Society of London and the French Academy of Sciences. Dr. Baltimore has served as a director of Amgen Inc. since 1999 and BB Biotech, AG since 2004. Dr. Baltimore was also a director of MedImmune, Inc. from 2003 to 2007. We believe that Dr. Baltimore possesses specific attributes that qualify him to serve as a member of our board of directors, including his extensive scientific knowledge and leadership positions at highly regarded research institutions. Dr. Baltimore holds a B.A. in Chemistry from Swarthmore College, a PhD from Rockefeller University and was a post-doctoral fellow at MIT and Albert Einstein College of Medicine.

Brook Byers has been a member of our board of directors since 2004. Mr. Byers has been a venture capital investor since 1972 and is a Managing Partner of Kleiner Perkins Caufield & Byers. He has been closely involved with more than 50 new technology-based ventures, many of which have already become public companies. He formed the first life sciences practice group in the venture capital profession in 1984 and led Kleiner Perkins Caufield & Byers to become a premier venture capital firm in the medical, healthcare and biotechnology sectors. Currently, Mr. Byers serves on the board of directors of Genomic Health, Inc. and seven private companies. We believe that Mr. Byers possesses specific attributes that qualify him to serve as a member of our board of directors, including his experience with growing multiple companies in the life sciences industry and his leadership in personalized medicine initiatives. Mr. Byers holds a B.S. degree in Electrical Engineering from the Georgia Institute of Technology and an M.B.A from Stanford University.

Michael Hunkapiller, PhD has been a member of our board of directors since 2005. Since November 2004, Dr. Hunkapiller has been a General Partner at Alloy Ventures, or Alloy, a venture capital firm. Prior to Alloy, Dr. Hunkapiller spent 21 years at Applied Biosystems. At Applied Biosystems, he held various positions, most recently serving as president and general manager. We believe that Dr. Hunkapiller possesses specific attributes that qualify him to serve as a member of our board of directors, including his experience at Applied Biosystems, where he helped grow the company from a startup to a public company with almost \$2 billion in annual revenue, leading groundbreaking innovations, including the development of the automated DNA sequencing systems used to sequence the human genome. He is member of the National Academy of Engineering. Dr. Hunkapiller holds a PhD in Chemical Biology from the California Institute of Technology and a B.S. in Chemistry from Oklahoma Baptist University.

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Randy Livingston has been a member of our board of directors since 2009. He has served as Vice President for Business Affairs and Chief Financial Officer of Stanford University since March 2001. Before joining Stanford, Mr. Livingston served as the executive vice president, chief financial officer and a director of OpenTV Corp. from 1999 to 2001. Before joining OpenTV in 1999, Mr. Livingston served as a consultant and part-time chief financial officer for Silicon Valley technology companies with such diverse specialties as genomics, Internet commerce, medical devices, chemical synthesis and enterprise software. Previously, he was director of corporate development at Apple Computer and chief financial officer for Taligent, a 400-employee Apple-IBM-Hewlett-Packard joint venture system software company. Mr. Livingston currently serves as a director of Genomic Health, Inc. and eHealth, Inc. We believe that Mr. Livingston possesses specific attributes that qualify him to serve as a member of our board of directors, including his executive experience and his financial and accounting expertise with public companies. Mr. Livingston holds a B.S. in Mechanical Engineering and an M.B.A. from Stanford University.

Susan Siegel has been a member of our board of directors since 2006. Since March 2007 she has been a General Partner at Mohr Davidow Ventures, a venture capital firm, where she leads investments in life sciences, healthcare and personalized medicine. Prior to joining MDV, Ms. Siegel was at Affymetrix, Inc. from April 1998 to April 2006. Ms. Siegel served as Affymetrix's Senior Vice President of Sales and Marketing until 1999 when she became President and in 2000 a member of the board of directors. We believe that Ms. Siegel possesses specific attributes that qualify her to serve as a member of our board of directors, including her experience of growing biotechnology companies for nearly 25 years by bringing key enabling technologies to the forefront of biomedical research and healthcare. Ms. Siegel holds a B.S. in Biology from the University of Puerto Rico and a M.S. in Biochemistry and Molecular Biology from Boston University Medical School.

David Singer has been a member of our board of directors since 2006. Since 2004 Mr. Singer has been a Limited Partner at Maverick Capital Ltd., a private investment firm, where he is responsible for the firm's private investments globally. Previously Mr. Singer was an entrepreneur, acting as the founding President and Chief Executive Officer of three healthcare companies, including Affymetrix, Inc. He currently serves on a number of private company boards and previously served on the board of directors of Affymetrix from 1993 to June 2008, Concept Therapeutics from 1998 to June 2008, and Oscient Pharmaceuticals from February 2004 to June 2006, and has served as the senior financial officer of two publicly traded companies. We believe that Mr. Singer possesses specific attributes that qualify him to serve as a member of our board of directors, including his executive experience and his financial and accounting experience with both public and private companies. Mr. Singer holds a B.A. from Yale University and an M.B.A. from Stanford University.

Board Composition

Our board of directors is currently composed of eight members. Six of our directors have been determined to be independent within the meaning of the independent director guidelines of The NASDAQ Stock Market. Immediately prior to this offering, our board of directors will be divided into three staggered classes of directors. At each annual meeting of stockholders, a class of directors will be elected for a three-year term to succeed the same class whose terms are then expiring. The terms of the directors will expire upon the election and qualification of successor directors at the annual meeting of stockholders to be held during the years 2011 for the Class I directors, 2012 for the Class II directors and 2013 for the Class III directors.

Our Class I directors will be Hugh Martin, Brook Byers and Susan Siegel.

Our Class II directors will be Michael Hunkapiller, Randy Livingston and David Baltimore .

Our Class III directors will be William Ericson and David Singer.

Our amended and restated certificate of incorporation and bylaws provide that the number of our directors shall be fixed from time to time by a resolution of the majority of our board of directors. Each officer serves at the discretion of the board of directors and holds office until his successor is duly elected and qualified or until his or her earlier resignation or removal. There are no family relationships among any of our directors or executive officers.

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The division of our board of directors into three classes with staggered three-year terms may delay or prevent a change of our management or a change of control. See *Description of Capital Stock – Anti-Takeover Effects of Delaware Law and Our Amended and Restated Certificate of Incorporation and Bylaws* for a discussion of other anti-takeover provisions found in our amended and restated certificate of incorporation and bylaws.

Director Independence

Upon the closing of this offering, our common stock will be listed on The NASDAQ Global Market. Under the rules of The NASDAQ Stock Market, independent directors must comprise a majority of a listed company's board of directors within a specified period of the closing of its initial offering. In addition, the rules of The NASDAQ Stock Market require that, subject to specified exceptions, each member of a listed company's audit, compensation and corporate governance and nominating committees be independent. Audit committee members must also satisfy the independence criteria set forth in Rule 10A-3 under the Securities Exchange Act of 1934, as amended. Under the rules of The NASDAQ Stock Market, a director will only qualify as an independent director if, in the opinion of that company's board of directors, that person does not have a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director.

In order to be considered to be independent for purposes of Rule 10A-3, a member of an audit committee of a listed company may not, other than in his or her capacity as a member of the audit committee, the board of directors or any other board committee: (1) accept, directly or indirectly, any consulting, advisory or other compensatory fee from the listed company or any of its subsidiaries; or (2) be an affiliated person of the listed company or any of its subsidiaries.

In July 2010, our board of directors undertook a review of its composition, the composition of its committees and the independence of each director. Based upon information requested from and provided by each director concerning his or her background, employment and affiliations, including family relationships, our board of directors has determined that none of Messrs. Byers, Ericson, Livingston and Singer, Dr. Hunkapiller and Ms. Siegel, representing six of our seven directors at that time, has a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director and that each of these directors is independent as that term is defined under the rules of The NASDAQ Stock Market. Our board of directors also determined that Messrs. Byers, Livingston and Singer, who comprise our audit committee, Mr. Ericson, Dr. Hunkapiller and Ms. Siegel, who comprise our compensation committee, and Messrs. Byers and Singer and Ms. Siegel, who comprise our nominating and corporate governance committee, satisfy the independence standards for those committees established by applicable SEC rules and the rules of The NASDAQ Stock Market. In making this determination, our board of directors considered the relationships that each non-employee director has with our company and all other facts and circumstances our board of directors deemed relevant in determining their independence, including the beneficial ownership of our capital stock by each non-employee director.

Board Committees

Our board of directors has an audit committee, a compensation committee and a corporate governance and nominating committee, each of which has the composition and the responsibilities described below. The audit committee, compensation committee and corporate governance and nominating committee all operate under charters approved by our board of directors, which charters will be available on our website upon the closing of this offering.

Audit Committee. Our audit committee oversees our corporate accounting and financial reporting process and assists the board of directors in monitoring our financial systems and our legal and regulatory compliance. Our audit committee is responsible for, among other things:

selecting and hiring our independent auditors;

appointing, compensating and overseeing the work of our independent auditors;

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approving engagements of the independent auditors to render any audit or permissible non-audit services;

reviewing the qualifications and independence of the independent auditors;

monitoring the rotation of partners of the independent auditors on our engagement team as required by law;

reviewing our financial statements and reviewing our critical accounting policies and estimates;

reviewing the adequacy and effectiveness of our internal controls over financial reporting; and

reviewing and discussing with management and the independent auditors the results of our annual audit, our quarterly financial statements and our publicly filed reports.

The members of our audit committee are Messrs. Byers, Livingston and Singer. Mr. Livingston is our audit committee chairman and was appointed to our audit committee on September 1, 2009. Our board of directors has determined that each member of the audit committee meets the financial literacy requirements under the rules of The NASDAQ Stock Market and the SEC and each of Messrs. Livingston and Singer qualifies as our audit committee financial experts as defined under SEC rules and regulations. Our board of directors has concluded that the composition of our audit committee meets the requirements for independence under the current requirements of The NASDAQ Stock Market and SEC rules and regulations. We believe that the functioning of our audit committee complies with the applicable requirements of The NASDAQ Stock Market and SEC rules and regulations.

Compensation Committee. Our compensation committee oversees our corporate compensation policies, plans and programs. The compensation committee is responsible for, among other things:

reviewing and recommending policies, plans and programs relating to compensation and benefits of our directors, officers and employees;

reviewing and recommending compensation and the corporate goals and objectives relevant to compensation of our Chief Executive Officer;

reviewing and approving compensation and corporate goals and objectives relevant to compensation for executive officers other than our Chief Executive Officer;

evaluating the performance of our executive officers in light of established goals and objectives;

developing in consultation with our board of directors and periodically reviewing a succession plan for our Chief Executive Officer; and

administering our equity compensations plans for our employees and directors.

The members of our compensation committee are Mr. Ericson, Dr. Hunkapiller and Ms. Siegel. Mr. Ericson is the chairman of our compensation committee. Our board of directors has determined that each member of our compensation committee is independent within the meaning of the independent director guidelines of The NASDAQ Stock Market. We believe that the composition of our compensation committee meets the

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requirements for independence under, and the functioning of our compensation committee complies with, any applicable requirements of The NASDAQ Stock Market and SEC rules and regulations.

Our compensation committee and our board of directors have approved a succession plan for our Chief Executive Officer.

Corporate Governance and Nominating Committee. Our corporate governance and nominating committee oversees and assists our board of directors in reviewing and recommending corporate governance policies and nominees for election to our board of directors. The corporate governance and nominating committee is responsible for, among other things:

evaluating and making recommendations regarding the organization and governance of the board of directors and its committees;

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assessing the performance of members of the board of directors and making recommendations regarding committee and chair assignments;

recommending desired qualifications for board of directors membership and conducting searches for potential members of the board of directors; and

reviewing and making recommendations with regard to our corporate governance guidelines.

The members of our corporate governance and nominating committee are Messrs. Byers and Singer and Ms. Siegel. Mr. Singer is the chairman of our corporate governance and nominating committee. Our board of directors has determined that each member of our corporate governance and nominating committee is independent within the meaning of the independent director guidelines of The NASDAQ Stock Market.

Our board of directors may from time to time establish other committees.

Director Compensation

The following table sets forth information concerning compensation paid or accrued for services rendered to us by members of our board of directors for the fiscal year ended December 31, 2009. The table excludes Mr. Martin and Dr. Turner, who are named executive officers and did not receive director compensation in the fiscal year ended December 31, 2009.

Name	Fees earned or paid in cash (\$)	Option awards (\$) ⁽¹⁾⁽³⁾	Total (\$)
Brook Byers			
William Ericson			
Michael Hunkapiller, PhD			
Susan Siegel			
David Singer			
Randy Livingston	17,500	105,600 ⁽²⁾	123,100

(1) Amounts shown represent the aggregate grant date fair value of the option awards computed in accordance with FASB Topic ASC 718. These amounts do not correspond to the actual value that will be recognized by the directors. The assumptions used in the valuation of these awards are consistent with the valuation methodologies specified in the notes to our financial statements.

(2) Mr. Livingston was granted an option on July 24, 2009 to purchase up to 80,000 shares of our common stock at a price per share of \$2.82. The option vests beginning on July 24, 2009 and vests as to 1/4th of the shares subject to the option after one year of the option commencement date, and as to 1/48th of the shares subject to the option per month for the subsequent three years, subject to Mr. Livingston's continued service through each vesting date.

(3) The aggregate number of shares subject to stock awards and stock options outstanding at December 31, 2009 for each director is as follows:

**Aggregate Number (#) of
Stock Awards Outstanding
as of December 31, 2009**

Name
Brook Byers

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William Ericson	
Michael Hunkapiller, PhD	
Susan Siegel	130,000
David Singer	
Randy Livingston	80,000

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Upon consummation of our initial public offering, non-employee directors will receive an annual retainer of \$35,000. The chair of our audit committee will be paid an additional annual retainer of \$20,000, and members of our audit committee other than the chair will be paid an additional annual retainer of \$10,000. The chair of our compensation committee will be paid an additional annual retainer of \$14,000, and members of our compensation committee other than the chair will be paid an additional annual retainer of \$7,000. The chair of our corporate governance and nominating committee will be paid an additional annual retainer of \$10,000, and members of our corporate governance and nominating committee other than the chair will be paid an additional annual retainer of \$5,000. Our lead independent director will be paid an additional annual retainer of \$15,000.

Our outside director equity compensation policy will become effective immediately upon the closing of this offering. The policy is intended to formalize the granting of equity compensation to our non-employee directors under the 2010 Outside Director Equity Incentive Plan. The policy provides for automatic and nondiscretionary grants of nonstatutory stock options subject to the terms and conditions of the policy and the 2010 Outside Director Equity Incentive Plan.

Under the policy, in connection with the pricing of this initial public offering, each non-employee director serving on our board of directors at the time of this offering will be automatically granted an option to purchase 50,000 shares of our common stock at the price per share at which such common stock is sold in this offering. Each non-employee director, who first becomes a non-employee director following the effective date of the first registration statement filed by us and declared effective with respect to any class of our securities, will be automatically granted a stock option to purchase 50,000 shares of our common stock on the date such person first becomes a non-employee director. A director who is an employee and who ceases to be an employee, but who remains a director will not receive such an initial award.

In addition, each non-employee director will be automatically granted an annual stock option to purchase 25,000 shares of our common stock on the date of each annual meeting beginning on the date of the first annual meeting that is held at least four months after such non-employee director received his or her initial award, provided such non-employee director continues to serve as a director through such date. Our audit committee chairperson will also be automatically granted an additional annual stock option to purchase 10,000 shares of our common stock on the date of each annual meeting beginning on the date of the first annual meeting that is held at least four months after such audit committee chairperson received his or her initial award.

The exercise price of all stock options granted pursuant to the policy will be equal to the fair market value of our common stock on the date of grant. The term of all stock options will be 10 years. Subject to the adjustment provisions of the 2010 Outside Director Equity Incentive Plan, initial awards, including such awards granted in connection with this offering, will vest over three years, with one third of the shares subject to the option vesting on the one year anniversary of the date of grant, and the remaining shares vesting monthly over the following two years, provided such non-employee director continues to serve as a director through each vesting date. Subject to the adjustment provisions of the 2010 Outside Director Equity Incentive Plan, the annual awards, including the additional annual awards to our audit committee chairperson, will vest monthly over one year, provided such non-employee director continues to serve as a director through each vesting date.

The administrator of the 2010 Outside Director Equity Incentive Plan in its discretion may change or otherwise revise the terms of awards granted under the outside director equity compensation policy.

In the event of a change in control, as defined in our 2010 Outside Director Equity Incentive Plan, with respect to awards granted under the 2010 Outside Director Equity Incentive Plan to non-employee directors, the participant non-employee director will fully vest in and have the right to exercise awards as to all shares underlying such awards and all restrictions on awards will lapse, and all performance goals or other vesting criteria will be deemed achieved at 100% of target level and all other terms and conditions met.

Code of Business Conduct and Ethics

We have adopted a code of business conduct that is applicable to all of our employees, officers and directors. In addition, we have adopted a code of ethics that is applicable to our chief executive and senior financial officers.

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Compensation Committee Interlocks and Insider Participation

None of the members of our compensation committee is an officer or employee of our company. None of our executive officers currently serves, or in the past year has served, as a member of the board of directors or compensation committee of any entity that has one or more executive officers serving on our board of directors or compensation committee.

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EXECUTIVE COMPENSATION

Compensation Discussion and Analysis

The following discussion and analysis of compensation arrangements of our named executive officers for 2009 and 2010 should be read together with the compensation tables and related disclosures set forth below. This discussion contains forward-looking statements that are based on our current considerations, expectations and determinations regarding future compensation programs. The actual amount and form of compensation and the compensation programs that we adopt may differ materially from current or planned programs as summarized in this discussion.

Overview

Our compensation program is overseen and administered by the compensation committee of our board of directors, which currently is comprised of William Ericson, who serves as the Chairman, Sue Siegel and Michael Hunkapiller. Each of Mr. Ericson, Dr. Hunkapiller and Ms. Siegel qualify as (i) an independent director under the rules of The NASDAQ Stock Market and (ii) as an outside director under Section 162(m) of the Internal Revenue Code of 1986, as amended, or the Code.

The compensation committee's goal is to ensure that the total compensation paid to our executive officers is fair, reasonable and competitive. Our compensation program is designed to attract talented individuals to lead, manage and operate all aspects of our business and reward and retain those individuals who continue to meet our high expectations over time. Our executive compensation program combines short- and long-term components, cash and equity in amounts and proportions that we believe are most appropriate to incentivize and reward our executive officers for achieving our objectives. Our executive compensation program is also intended to make us competitive in our industry, where there is considerable competition for talented executives.

Objectives and Principles of Our Executive Compensation

The guiding principle in the development of our compensation strategy is to create and nurture a pay-for-performance culture, where exceptional company and individual performance contribution has the potential to be matched with appropriate financial rewards for the whole compensation package. The objectives of our compensation program are:

to attract the best and brightest employees;

to motivate successful execution of our corporate objectives;

to ensure that broad-based compensation programs are aligned with company objectives that when achieved will lead to an increase in value for our stockholders; and

to ensure retention of key staff.

Our current compensation programs reflect our startup origins in that they consist primarily of salary and stock options for our executive officers. We anticipate increasing the flexibility and elements of our compensation structure going forward, while striving to maintain transparency, simplicity and a clear pay-for-performance orientation. As our needs evolve, we intend to continue to evaluate our philosophy and compensation programs as circumstances require, and we will review executive compensation annually. We anticipate making new equity awards and adjustments to the components of our executive compensation program in connection with our yearly compensation review, which will be based, in part, upon the market analysis performed by the compensation consultant retained by our compensation committee, Radford.

Role of Compensation Consultant

Our compensation committee has the authority to engage the services of outside consultants to assist it in making decisions regarding the establishment of our compensation programs and philosophy. Our compensation committee retained Radford as its compensation consultant in 2010 to advise the compensation committee in

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matters related to executive and equity compensation. Radford reviewed and compiled data from companies in our peer group, as discussed below, and presented them to our compensation committee to assist it in determining our executive compensation.

Role of Executive Officers in Compensation Decisions

For executive officers other than our Chief Executive Officer, our compensation committee has historically sought and considered input from our Chief Executive Officer regarding such executive officers' responsibilities, performance and compensation. Specifically, our Chief Executive Officer recommends base salary increases and equity award levels that are used throughout our compensation plans, and advises our compensation committee regarding the compensation program's ability to attract, retain and motivate executive talent. These recommendations reflect compensation levels that our Chief Executive Officer believes are qualitatively commensurate with an executive officer's individual qualifications, experience, responsibility level, functional role, knowledge, skills and individual performance, as well as our company's performance. Our compensation committee considers our Chief Executive Officer's recommendations, and approves the specific compensation for all the executive officers. Our compensation committee also relies on the experience of our directors affiliated with venture capital firms, which have representatives on the board of directors of numerous private companies, in determining and approving the specific compensation amounts.

Our compensation committee meets in executive session, and our Chief Executive Officer does not attend compensation committee discussions where recommendations are made regarding his compensation. Our compensation committee applies a similar pay-for-performance philosophy when setting compensation for our Chief Executive Officer. Our compensation committee discusses with the Chief Executive Officer the core metrics to drive the business forward, and how various forms of variable and incentive compensation can be applied at the executive level to achieve our goals. When setting the structure of compensation for Mr. Martin, our compensation committee discusses the balance between near-term and long-term performance in structuring Mr. Martin's compensation. Mr. Martin does not provide input into setting his level of pay, which is under the purview of the compensation committee and board of directors. He also abstains from voting in sessions of the board of directors where the board of directors acts on the compensation committee's recommendations regarding his compensation.

Peer Group

In May 2010, based on the recommendation of our executive compensation consultant, our compensation committee adopted a peer group of companies. We have chosen our peer group from companies in both information technology and life sciences because our business requires skill sets from both industries. We used the following criteria in selecting a peer group:

companies with a similar industry focus;

companies with revenue between \$100,000,000 and \$500,000,000;

companies located near life sciences/technology hub markets which influence pay levels; and

companies with headcount generally between 200 to 1,000 staff members.

We also examined the practices of the peer group with a focus on the compensation arrangements, plans and practices of the companies that had gone public in the past three years to ensure our practices are in line with current industry standards.

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Our peer group for 2010 is comprised of following companies:

3PAR, Inc.