PACIFIC BIOSCIENCES OF CALIFORNIA INC
Form S-1/A
October 05, 2010
Table of Contents

As filed with the Securities and Exchange Commission on October 4, 2010

Registration No. 333-168858

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

AMENDMENT NO. 3 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	**3826**	**16-1590339**
(State or other jurisdiction of incorporation or organization)	*(Primary Standard Industrial Classification Code Number)*	*(I.R.S. Employer Identification Number)*

1380 Willow Road

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

1380 Willow Road

Menlo Park, CA 94025

(650) 521-8000

(Name, address, including zip code, and telephone number, including area code, of agent for service)

Copies to:

Larry W. Sonsini	**Matthew B. Murphy**	**Alan F. Denenberg**
Donna M. Petkanics	**Vice President and General Counsel**	**Davis Polk & Wardwell LLP**
Wilson Sonsini Goodrich & Rosati, P.C.	**1380 Willow Road**	**1600 El Camino Real**
650 Page Mill Road	**Menlo Park, CA 94025**	**Menlo Park, CA 94025**
Palo Alto, California 94304	**(650) 521-8000**	**(650) 752-2000**
(650) 493-9300		

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. ¨ _____

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 x (Do not check if a smaller reporting company)	Smaller reporting company ¨

CALCULATION OF REGISTRATION FEE

Title of Each Class of Securities to be Registered	**Proposed Maximum Offering Price Per Share**	**Proposed Maximum Aggregate Offering Price[(1)]**	**Amount of Registration Fee[(2)]**
Common Stock, par value $0.0001 par share	$17.00	$230,000,000	$16,399.00

(1) Estimated solely for the purpose of calculating the registration fee in accordance with Rule 457(o) under the Securities Act of 1933, as amended. Includes offering price of shares that the underwriters have the option to purchase to cover over-allotments.

(2) The Registrant previously paid this registration fee in connection with the previous filings of this Registration Statement.

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.

Table of Contents

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 October 4, 2010

12,500,000 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 $15.00 and $17.00 per share.

We have applied to list our common stock on the NASDAQ Global Market under the symbol PACB .

	Per share	*Total*
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 1,875,000 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

Table of Contents

Table of Contents

Table of Contents

Table of Contents

TABLE OF CONTENTS

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.

Table of Contents

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.

Table of Contents

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 a report commissioned on our behalf and conducted by Scientia Advisors, a life sciences consulting firm. The growth in this market is expected to be driven by increases in the demand for sequencing products from both research institutions and commercial companies, including 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

Table of Contents

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 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.

Table of Contents

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 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 may reflect the presence of DNA methylation. The PacBio *RS* detects changes in kinetics automatically by capturing and recording changes in the duration of, and distances between, each of the fluorescent pulses during a typical sequencing analysis. We and our collaborators have demonstrated that this information may be a sensitive measure of chemical modification of nucleotides such as methylation. Although the PacBio *RS* currently records the information required to perform this analysis during a standard sequencing run, we plan to offer kinetic detection analysis as an application through future software and consumable upgrades. First and second generation sequencing systems are unable to accurately record this type of kinetic data because the flush and scan sequencing process disrupts the timing of the natural incorporation process. In addition, the use of multiple molecules prevents this information from being collected as it cannot be observed in aggregate.

Table of Contents

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, 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;

Table of Contents

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;

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;

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 this prospectus are the property of their respective owners.

Table of Contents

THE OFFERING

Common stock offered by us	12,500,000 Shares
Over-allotment option	1,875,000 Shares
Common stock to be outstanding after this offering	50,113,504 Shares (or 51,988,504 shares if the underwriters exercise their over-allotment option in full)
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 37,613,504 shares of our common stock outstanding as of June 30, 2010 and excludes:

- 8,787,672 shares of common stock issuable upon the exercise of options outstanding as of June 30, 2010, with a weighted-average exercise price of $5.42 per share;
- 25,282 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 preferred share that upon the closing of this offering will represent warrants to purchase shares of common stock at a weighted-average exercise price of $3.16 per common share; and
- 5,768,602 shares of our common stock reserved for future issuance under our stock-based compensation plans, including 2,500,000 shares of common stock reserved for issuance under our 2010 Equity Incentive Plan, 750,000 shares of our common stock reserved for issuance under our 2010 Employee Stock Purchase Plan, 500,000 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 36,652,735 of shares of common stock upon the closing of this offering;

the conversion of all outstanding warrants to purchase shares of our convertible preferred stock into warrants to purchase 25,282 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.

The information in this prospectus also reflects the 1-for-2 reverse stock split of our outstanding common stock effected in September 2010.

Table of Contents

SUMMARY FINANCIAL DATA

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 consolidated financial data table reflects the 1-for-2 reverse stock split of our outstanding common stock effected in September 2010. 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 June 30,	
	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)]	$ (272.93)	$ (133.82)	$ (173.03)	$ (75.39)	$ (99.58)
Weighted-average shares outstanding used to calculate basic and diluted net loss per share[(1)]	78,841	326,955	506,865	465,755	633,019
Pro forma basic and diluted net loss per share (unaudited)[(1)]			$ (3.16)		$ (2.02)
Pro forma weighted-average shares outstanding used to calculate basic and diluted net loss per share (unaudited)[(1)]			27,738,744		31,202,612

(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.

Table of Contents

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 12,500,000 shares of common stock in this offering at an assumed initial public offering price of $16.00 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		
	Actual	Pro forma[1] (unaudited) (in thousands)	Pro forma as adjusted[2][3]
Balance sheet data:			
Cash, cash equivalents and investments	$ 138,756	$ 138,756	$ 321,256
Working capital	123,896	123,896	306,396
Total assets	152,897	152,897	335,397
Convertible preferred stock warrant liability	282		
Convertible preferred stock	367,036		
Total stockholders equity (deficit)	(235,650)	131,668	314,168

(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 12,500,000 shares of our common stock in this offering at an assumed initial public offering price of $16.00 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 $16.00 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 $11.6 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 $14.9 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 $14.9 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.

Table of Contents

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.

Table of Contents

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 66. 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

Table of Contents

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

Table of Contents

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

Table of Contents

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

Table of Contents

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

Table of Contents

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.

Table of Contents

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.

Table of Contents

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

Table of Contents

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

Table of Contents

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.

Table of Contents

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, some of our licenses from third parties limit the field in which we can use the licensed technology. Therefore, in order for us to use such licensed technology in potential future applications that are outside the licensed field of use, we may be required to negotiate new licenses with our licensors or expand our rights under our existing licenses. We can not assure you that we will be able to obtain such licenses or expanded rights on reasonable terms or at all. In addition, we have limited rights to participate in the prosecution and enforcement of the patents and patent applications that we have licensed. As a result, we cannot be certain that these patents and applications will be prosecuted and enforced in a manner consistent with the best interests of our business. Further, because of the rapid pace of technological change in our industry, we may need to rely on key technologies developed or licensed by third parties, and we may not be able to obtain licenses and technologies from these third parties at all or on reasonable terms. The occurrence of these events may have a material adverse effect on our business, financial condition or results of operations.

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

In addition to patents, we also rely upon trademarks, trade secrets, copyrights and unfair competition laws, as well as license agreements and other contractual provisions, to protect our intellectual property and other proprietary rights. Despite these measures, any of our intellectual property rights could be challenged, invalidated, circumvented or misappropriated. In addition, we attempt to protect our intellectual property and proprietary information by requiring our employees, consultants and certain academic collaborators to enter into confidentiality and assignment of inventions agreements, and by requiring our third-party manufacturing partners to enter into confidentiality agreements. There can be no assurance, however, that such measures will provide adequate protection for our intellectual property and proprietary information. These agreements may be breached, and we may not have adequate remedies for any such breach. In addition, our trade secrets and other proprietary information may be disclosed to others, or others may gain access to or disclose our trade secrets and

Table of Contents

other proprietary information. Enforcing a claim that a third party illegally obtained and is using our trade secrets is expensive and time consuming, and the outcome is unpredictable. Additionally, others may independently develop proprietary information and techniques that are substantially equivalent to ours. The occurrence of these events may have a material adverse effect on our business, financial condition or results of operations.

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

Our pending, issued and granted U.S. and foreign patents and patent applications have been, and may in the future be, subject to challenges by third parties asserting prior invention by others or invalidity on various grounds, through proceedings, such as interferences, reexamination or opposition proceedings. 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

Table of Contents

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,

Table of Contents

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,

Table of Contents

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 50,113,504 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 37,613,504 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 33,540,284 common stock, or 89.2% based on shares outstanding as of June 30, 2010, and holders of warrants to purchase 25,282 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

Table of Contents

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 16,835,619 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 43.6% 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 42.0% 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 approximately 948,000,000 shares of authorized but unissued shares of common stock;

Table of Contents

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 948,000,000 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.

Table of Contents

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, ex 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.

Table of Contents

USE OF PROCEEDS

We estimate that the net proceeds from our sale of 12,500,000 shares of common stock in this offering at an assumed initial public offering price of $16.00 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 $182.5 million, or $210.4 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 $11.6 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 36,652,735 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 25,282 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 12,500,000 shares of common stock in this offering at an assumed initial public offering price of $16.00 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 following table also reflects the 1-for-2 reverse stock split of our outstanding common stock effected in September 2010.

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		
	Actual	Pro forma	Pro forma as adjusted[1]
		(in thousands)	
Facility financing obligation, less current portion	$ 2,955	$ 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, 960,769 shares issued and outstanding, actual; 1,000,000,000 shares authorized, 37,613,504 shares issued and outstanding, pro forma; and 1,000,000,000 shares authorized, 50,113,504 shares issued and outstanding, pro forma as adjusted		4	5
Additional paid-in capital[1]	19,395	386,709	569,208
Accumulated other comprehensive income (loss)	(5)	(5)	(5)
Accumulated deficit	(255,040)	(255,040)	(255,040)
Total stockholders equity (deficit)[1]	(235,650)	131,668	314,168
Total capitalization[1]	$ 134,623	$ 134,623	$ 317,123

(1) A $1.00 increase (decrease) in the assumed initial public offering price of $16.00 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 $11.6 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

Table of Contents

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 additional paid-in capital, total stockholder equity and total capitalization by approximately $14.9 million. Similarly, each decrease of 1.0 million shares in the number of shares offered by us would decrease additional paid-in capital, total stockholders equity and total capitalization by approximately $14.9 million.

The number of shares of our common stock that will be outstanding following this offering is based on 37,613,504 shares of our common stock outstanding as of June 30, 2010 and excludes:

8,787,672 shares of common stock issuable upon the exercise of options outstanding as of June 30, 2010, with a weighted-average exercise price of $5.42 per share;

25,282 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 preferred share that upon the closing of this offering will represent warrants to purchase shares of common stock at a weighted-average exercise price of $3.16 per common share; and

5,768,602 shares of our common stock reserved for future issuance under our stock-based compensation plans, including 2,500,000 shares of common stock reserved for issuance under our 2010 Equity Incentive Plan, 750,000 shares of our common stock reserved for issuance under our 2010 Employee Stock Purchase Plan, 500,000 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.

Table of Contents

DILUTION

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 $(245.27) 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 $3.50 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 12,500,000 shares of common stock in this offering at an assumed initial public offering price of $16.00, 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 $314.2 million, or $6.27 per share of common stock. This represents an immediate increase in pro forma as adjusted net tangible book value of $2.77 per share to existing stockholders and an immediate dilution of $9.73 per share to new investors.

The following table illustrates this dilution on a per share basis after giving effect to the 1-for-2 reverse stock split of our outstanding common stock effected September 2010.

Assumed initial public offering price per share		$ 16.00
Pro forma net tangible book value per share as of June 30, 2010	$ 3.50	
Increase per share attributable to this offering	2.77	
Pro forma as adjusted net tangible book value per share after this offering		6.27
Pro forma net tangible book value dilution per share to new investors in this offering		$ 9.73

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 $3.86 per share, and the pro forma net tangible book value after this offering would have been $361.7 million, or $6.14 per share, causing dilution to new investors of $9.86 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 $6.41 per share, representing an immediate increase to existing stockholders of $2.91 per share and an immediate dilution of $9.59 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 $16.00, 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
	Number	Percent	Amount	Percent	Per share
Existing stockholders	37,613,504	75.1%	$ 367,876,401	64.8%	$ 9.78
New investors	12,500,000	24.9	200,000,000	35.2	16.00
Total	50,113,504	100.0%	$ 567,876,401	100.0%	$ 11.33

32

Table of Contents

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 if the underwriters exercise their over-allotment option in full, 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 assumed initial public offering price of $16.00, 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	37,613,504	72.3%	$ 367,876,401	61.5%	$ 9.78
New investors	14,375,000	27.7	230,000,000	38.5%	16.00
Total	51,988,504	100.0%	$ 597,876,401	100.0%	$ 11.50

The foregoing calculations are based on 37,613,504 shares of our common stock outstanding as of June 30, 2010 and exclude:

8,787,672 shares of common stock issuable upon the exercise of options outstanding as of June 30, 2010, with a weighted-average exercise price of $5.42 per share;

25,282 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 preferred share that upon the closing of this offering will represent warrants to purchase shares of common stock at a weighted-average exercise price of $3.16 per common share; and

5,768,602 shares of our common stock reserved for future issuance under our stock-based compensation plans, including 2,500,000 shares of common stock reserved for issuance under our 2010 Equity Incentive Plan, 750,000 shares of our common stock reserved for issuance under our 2010 Employee Stock Purchase Plan, 500,000 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.

Table of Contents

SELECTED FINANCIAL DATA

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.

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

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

	Years ended December 31,					Six-month periods ended June 30,	
	2005	2006	2007	2008	2009	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]	(*)	(*)	$ (272.93)	$ (133.82)	$ (173.03)	$ (75.39)	$ (99.58)
Weighted-average shares outstanding used to calculate basic and diluted net loss per share[2]		996	78,841	326,955	506,865	465,755	633,019
Pro forma net loss per share basic and diluted (unaudited)[2]					$ (3.16)		$ (2.02)
Pro forma weighted-average shares outstanding used to calculate net loss per share basic and diluted (unaudited)[3]					27,738,744		31,202,612

Table of Contents

	As of December 31,					June 30,
	2005	2006	2007	2008	2009	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.

Table of Contents

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.

Table of Contents

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.

Table of Contents

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.

Table of Contents

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 June 30,	
	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.

Table of Contents

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 June 30, (unaudited)	
	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

Table of Contents

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.

Table of Contents

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	731,250	$ 3.86	$ 3.86	$ 1.78
April 21, 2009	21,500	$ 3.86	$ 3.86	$ 1.80
May 19, 2009	20,000	$ 3.86	$ 3.86	$ 1.82
June 10, 2009	252,500	$ 5.64	$ 5.64	$ 2.72
July 21, 2009	103,000	$ 5.64	$ 5.64	$ 2.62
July 24, 2009	165,000	$ 5.64	$ 5.64	$ 2.64
December 15, 2009	493,000	$ 8.50	$ 8.50	$ 3.90
February 3, 2010	1,101,777	$ 8.50	$ 8.50	$ 4.00
February 17, 2010	547,500	$ 8.50	$ 8.50	$ 4.00
February 22, 2010	375,000	$ 8.50	$ 8.50	$ 4.01
June 8, 2010	473,750	$ 10.84	$ 10.84	$ 5.54
June 9, 2010	100,000	$ 10.84	$ 10.84	$ 5.54
July 8, 2010	37,250	$ 12.74	$ 12.74	$ 6.64
July 19, 2010	286,500	$ 12.74	$ 12.74	$ 6.64
July 29, 2010	180,000	$ 12.74	$ 12.74	$ 6.64
August 4, 2010	109,291	$ 13.42	$ 13.42	$ 7.00
August 12, 2010	250,000	$ 13.42	$ 13.42	$ 7.00
September 21, 2010	55,000	$ 13.50	$ 13.50	$ 7.03

(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 $93.1 million based on the estimated value of $16.00 per share, the midpoint of the planned range of this offering.

We granted stock options with exercise prices between $8.50 and $13.50 per share during 2010 while stock options with exercise prices between $3.86 and $8.50 per share were granted during 2009. No single event caused the valuation of our common stock to increase or decrease from January 2009 to September 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 $3.86 per share compared to the previous estimate of $6.96 per share in December 2008.

Table of Contents

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 $5.64 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 $8.50 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 $10.84 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

Table of Contents

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 $12.74 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 $13.42 per share.

September 2010. During August 2010, the U.S. capital markets and equity values of our peer group recovered relative to the preceding measurement resulting in modest improvements in multiples used in our valuation assessments and our conclusions of enterprise value.

The PWERM allocation method employed an adjusted CAPM discount rate of 24%, a marketability discount to specified events of 6% to 27% based on the average estimated time to each event ranging from 0.24 to 4.4 years. The expected outcomes were weighted 95% towards IPO scenarios occurring during late 2010 and early 2011 and 5% to remaining a private operating company. For options granted during September 2010, we estimated the fair value of our common stock to be $13.50 per share.

While the midpoint of the currently estimated range of the initial public offering price of $16.00 per share is greater than the most recent value of common stock of $13.50 per share determined by our board of directors in connection with the grant of stock options, there are several factors noted above that explain this difference. In the first quarter of 2010, we secured multiple orders for the limited production release of the PacBio *RS*, as well as commenced selling of our full commercial release version. During the second and third quarters of 2010 we closed three financing rounds of our Series F preferred stock at a per share price of $15.26 per preferred share which, in addition to providing a valuation milestone, eliminated certain short-term financing risks. Also in the third quarter we commenced shipments of our limited production release PacBio *RS* instruments. Our prospects and expectations of growth continued to improve and our outlook regarding the fair market value of our common stock under various initial public offering and sale scenarios improved. In July 2010 we held our organizational meeting for our initial public offering; in August 2010 we filed the registration statement of which this prospectus is a part; and in September 2010 we filed our first and second amendment to the registration statement. All of these actions signaled that an initial public offering was becoming more likely, which would result in liquidity for the common stock and elimination of the superior rights and preferences of the preferred stock. This positively affected assumptions of the expected type, timing and likelihood of possible liquidity scenarios. The estimated initial public offering price range necessarily assumes that the initial public offering has occurred, a public market for our common stock has been created and that our preferred stock has converted into common stock in connection with the initial public offering, and therefore excludes any marketability or illiquidity discount for our common stock and excludes the superior rights and preferences of our preferred stock, which were appropriately taken into account in the board s fair market value determination in September 2010.

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

Table of Contents

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.

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.

Table of Contents

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 million, $2.0 million, 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 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,		Increase/ (decrease)	% Increase/ (decrease)
	2009	2010		
	(unaudited)			
	(in thousands, except percentages)			
Revenue	$	$ 1,174	$ 1,174	&nb