PACIFIC BIOSCIENCES OF CALIFORNIA INC
Form 424B1
October 27, 2010
Table of Contents

Filed Pursuant to Rule 424(b)(1)
Registration No. 333-168858

Prospectus

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 $16.00 per share.

Our common stock has been approved for listing on the NASDAQ Global Select Market under the symbol PACB .

	Per share	*Total*
Initial public offering price	**$ 16.00**	**$ 200,000,000**
Underwriting discounts and commissions	**$ 1.12**	**$ 14,000,000**
Proceeds to Pacific Biosciences, before expenses	**$ 14.88**	**$ 186,000,000**

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 November 1, 2010.

J.P.Morgan **Morgan Stanley**

Deutsche Bank Securities **Piper Jaffray**

October 26, 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 November 20, 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.
NASDAQ Global Select 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 the initial public offering price of $16.00 per share, after deducting 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]
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		